Vol.1, No.2, May-2023

APPLIED SCIENCES RESEARCH PERIODICALS

TABLE OF CONTENTS

EDITORIAL BOARD

DISCLAIMER

All the manuscripts are published in good faith and intentions to promote and encourage research around the globe. The contributions are property of their respective authors/owners and Applied Sciences Research Periodicals (ASRP) is not responsible for any content that hurts someone's views or feelings. Authors are responsible for if any plagiarism is found in published material.

Applied Sciences Research Periodicals
May 2023, Vol. 1, No. 2, pp. 01-04

The Mechanism of Brain Strokes and Heart Attacks May Be the Same

Ermoshkin Vladimir Ivanovich

1. RosNOU, Moscow

Abstract:
Goals: The main goal of all researchers of atherosclerosis, strokes and heart attacks is the same - to find the cause and mechanism of these diseases. Thanks to this, in the near future, it may be possible to postpone the onset of old age, reduce the number of cardiovascular diseases, and increase the duration of an active human life. Method: Studying information on the Internet, participating in medical conferences, publishing articles. Results: In 2020, the cause of atherosclerosis was found: due to deformation (spasm) of the arteries due to loss of arterial blood volume. As further studies have shown, the discovered mechanism of atherosclerosis, as a response of the walls of the arteries to stress, is the main cause of many dangerous human diseases.

THE POSITION OF OFFICIAL MEDICINE ON HEART ATTACK AND BRAIN STROKE

Stroke and cardiovascular diseases are the two main causes of death in the world [1].

Other studies of recent decades [2] have demonstrated a close relationship between cardiac and cerebral pathology resulting from various cardiovascular diseases. In general, with a thorough examination, cardiac changes are detected in 75-80% of patients suffering from vascular pathology of the brain.

There are common pathogenetic mechanisms and risk factors [3] that cause simultaneous development of myocardial infarction and ischemic stroke, due to decompensation of systemic or regional blood circulation. Arterial hypertension is one of the main risk factors for myocardial infarction and ischemic stroke. In clinical studies, a direct correlation has been repeatedly proven between the risk of myocardial infarction, coupled with acute cerebrovascular accident and blood pressure levels.

It is known that everyone has atherosclerosis at one stage or another of its development. Atherosclerosis is a chronic vascular pathology that appears due to an imbalance in the metabolism of fats and proteins in the body and is accompanied by the accumulation of lipids with subsequent proliferation of connective tissue fibers in the vascular wall. The progression of atherosclerosis is accompanied by a violation of the elastic properties of the vessel, its deformation, narrowing of the lumen, and, consequently, a violation of patency for blood flow. (There are more than a dozen "theories" of atherosclerosis in medicine, but there has not been a unified theory of its occurrence at the moment.)

THE AUTHOR'S NEW THEORY OF ATHEROSCLEROSIS AND OTHER DISEASES

It is the pathological spasm of the arteries and subsequent atherosclerosis that shorten a person's life expectancy. But why do periodic spasms occur?

In 2020, a revolutionary theory of atherosclerosis appeared [4-7]. Of course, with atherosclerosis, no genetic metabolic disorder occurs in the vessels. The main thing is stress and low physical activity. When the level of blood pressure (BP) rises, large arteriovenous anastomoses (AVA) can open. This leads to the fact that in stressful situations, blood leaks from the arterial pool to the venous pool occur, while blood pressure decreases for a while. The volume of blood in the arteries decreases, and in the veins increases. And this is despite the fact that the left and right hearts throw out the same portions of blood with each beat. With continued stress, the decreasing volume of blood leads to spasm of both large and small arteries, because the volume of the arterial bed should exactly coincide with the volume of arterial blood. Blood behaves like a Newtonian viscous incompressible fluid. The arterial bed has elastic thick multilayer walls, and the walls have their own circulatory system.

Someday there comes a moment when the vessels of the arms and legs are subjected to spasm, the latter become cold. Further, if nothing is done, blood loss increases, a significant spasm spreads to all the arteries. Blood pressure is increasing, arterial blood loss is also increasing, blood pressure adjustments are going into "disarray", because it is becoming increasingly difficult to provide the necessary perfusion of cerebral or coronary circulation with a small volume of arterial blood, a hypertensive crisis with signs of a transient ischemic attack or a hypertensive crisis with signs of angina pectoris may occur. Both diseases may occur simultaneously. Who will be lucky, but there is one reason: a lack of arterial blood can lead to a hypertensive crisis with blood pressure up to 180-220 mm Hg.

The greatest influence of the general spasm (i.e., the decrease in the lumen of the arteries) falls on the walls of the arteries near and above the heart, especially in the areas of bifurcations, bends and other inhomogeneities of the arteries. This is because the pulse wave with negative pressure, following the wave with positive pressure, is the most "powerful" near the heart. The pulse wave in case of blood leaks "works" in the dangerous direction of "collapse of the walls" of some arteries.

Generally speaking, when there is a lack of blood, the multilayer walls of the arteries deform, they are stressed, they go into a non-equilibrium state during periods of diastole. The walls reduce the internal lumen of the vessel, they stretch in the transverse direction with a fixed size of the rigid outer layer (adventitia). In the middle muscle layer of the walls, due to the expansion of the volume of the walls, a pressure drop is created, stretching of muscle fibers and suction of fluid from the outside. Yes, that's right: stretched layers suck liquids inside the walls! Through the "holes" in the unicellular endothelium, the penetration of the smallest fractions of blood that are contained in arterial blood occurs. These fractions primarily include lipoproteins. It is the physical forces of absorption that "force" small lipoprotein molecules to penetrate into the walls of the arteries and "fix" there. In the zone of "fixing of foreign bodies" the inflammatory process begins. This is how atherosclerosis and plaques are formed. In parallel, varicose veins and blood clots may occur in the veins of the lower half of the body due to slowing down of movement and stagnation of the increased volume of venous blood.

Another reason for atherosclerosis is the "verticality" of the main arteries, including the aorta, of a person. A vertical column of fluid for an upright person creates forces of separation of the inner layer from the muscular layer of the artery, especially in the upper part of each vertically located artery. The inner layer (endothelium) gradually becomes tougher, because it is more often damaged, exfoliates, so traces of damage remain on it. Looking at the drawings of the aortic

incision of an adult, we can see where the greatest separation forces are created (on average): this is the upper side of the aortic arch! And this is what PHYSICS tells us! These forces are more powerful in tall people!

Thus, as the degree of systemic atherosclerosis increases in humans, the ischemia of many organs increases, including the myocardium, the brain, and other organs. Of course, ischemia of each organ has its own characteristics in terms of mental and physical effects on a person.

The main difference between which bouquet of diseases a person lives his life with is genetics, lifestyle, nutrition, climate, education, regularity of physical activity, etc.

Obviously, if the root cause of ischemic strokes and transient ischemic attacks [8, 9], on the one hand, and the root cause of angina and heart attack, on the other hand, are the same, namely, a decrease in arterial blood volume during stress and subsequent forced arterial spasm, then these two types of diseases will have a high degree of correlation among themselves. And not only brain and heart diseases are interconnected, but also other pairs: heart and kidneys, brain and kidneys, brain and lungs, cardiac fibrillation and cerebral ischemia...

Official medicine has not been able to explain the confirmation of significant correlations in these pairs for decades. This effect in modern medicine is shamefully disguised under the term "comorbidity" of many diseases or under the term "multifactorial" causes.

Meanwhile, the institute's medical scientists are looking for (and finding!?) signaling (toxic) molecules that transmit information about a "disaster" from one organ to other organs [1-3], but do not notice the main, common pathological cause for all organs.

CONCLUSIONS

This article is a description of the hypothesis of the relationship between brain strokes and heart attacks. So, why do CVD arise – there has been progress. How to treat patients - in accordance with the now known mechanism of CVD.

The opinion of Official Medicine for March 2023 is unshakable: most of the main human diseases are diseases with multifactorial causes, with significant comorbidity.

According to the New Theory, the main and ONLY cause is stress, which creates a shortage in the arterial bloodstream due to its leakage into the veins during periods of stress.

I suggest that medical scientists consider this hypothesis on its merits. E-mail at the top.

I (the physicist) hope that there will be brave medical scientists. And they will be able to interest or convince gray-haired academicians to change the institute's scientific plans at their scientific and technical councils. It is necessary to recognize the plausibility of the proposed hypothesis, to begin research. Meanwhile, the incidence of CVD, strokes and heart attacks continue to break records all over the world, and especially in Russia.

If there are people who are influential "at the top", regardless of their education and position, then I ask them to put in a word about a new theory where it will be appropriate. My efforts, at least

since 2020, in this direction give "zero" result. Some say that in medicine you have to wait 50 years until there are no opponents left.

REFERENCES

1. Ganekar S., Kori S., Lippert T. et al. Pathological links between stroke and cardiac arrest. Neurosurgeon Chin Jl 2, 40 (2016). https://doi.org/10.1186/s41016-016-0056-1

2. Fonyakin A.V., Geraskina L.A. Therapy of heart diseases in vascular pathology of the brain. RMZH. 2005; 22:1477.

3. Chichkova M.A., Kozlova O.S., Ajigitov A.Yu., Chichkov A.M. CLINICAL PREDICTORS OF THE DEVELOPMENT OF ACUTE ISCHEMIC STROKE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION // Modern problems of science and education. – 2016. – № 5.

4. Ermoshkin Vladimir Ivanovich. "The Mechanism of Atherosclerosis and Pathological Spasms of Human Arteries". EC Cardiology 7.9 (2020): 69-74. https://ecronicon.com/eccy/ECCY-07-00750.php

4. Vladimir Ermoshkin. "Possible Cause of Atherosclerosis from the Point of View of a Physicist". EC Cardiology 8.6 (2021): 24-28.

6. Ermoshkin V. I. "Eurasian Scientific Association", "Atherosclerosis occurs due to loss of arterial blood", No. 9 (67) • September, 2020. https://esa-conference.ru/wp-content/uploads/2020/10/esa-september-2020-part3.pdf

7. Vladimir Ivanovich Ermoshkin. Atherosclerosis Immediate Prospects. J Clin Cardio & Case Res, 2021, 1: 1-2.

8. Internet Russian resource. V. I. Ermoshkin "What is the difference between a transient ischemic attack and an ischemic stroke?" Medlinks - 02/26/2023 http://www.medlinks.ru/article.php?sid=104141&query=%E5%F0%EC%EE%F8%EA%E8%ED

9. Ermoshkin Vladimir Ivanovich. "The Cause of Transient Ischemic Attacks". EC Cardio

Applied Sciences Research Periodicals
May 2023, Vol. 1, No. 2, pp. 05-10

Adolescent Mental Health in the Wake of Parental Bankruptcy: Exploring the Impact of Greece's Economic Crisis

Maria Maniou

1. Nursing Department, Hellenic Mediterranean University, Heraklion, Greece

Abstract:
This mini review examines the impact of parental bankruptcy on the mental health of adolescents in Greece in the context of the country's ongoing economic crisis. Results from the reviewed studies indicate that adolescent mental health is significantly affected by parental bankruptcy, with higher rates of depression, anxiety, and stress reported among teenagers with bankrupt parents. Factors such as economic hardship, family conflict, and social stigma are found to exacerbate the negative impact of parental bankruptcy on adolescent mental health. Based on our review, we highlight the need for continued research on this topic and call for the development of targeted interventions to support the mental health of adolescents in Greece during this challenging time.

Keywords: adolescent mental health, parental bankruptcy, economic crisis, Greece, entrepreneurship

INTRODUCTION

The economic crisis that hit Greece in 2008 had severe repercussions on the country's society, with a significant impact on adolescent mental health. One of the most significant consequences of the crisis was the widespread occurrence of parental bankruptcy, leading to financial insecurity and stress within the family. The present mini-review aims to explore the impact of Greece's economic crisis on adolescent mental health in the wake of parental bankruptcy.

Adolescence is a critical period of development, where individuals undergo significant physical, cognitive, and emotional changes. It is a time when young people are particularly vulnerable to stress and adversity, and parental bankruptcy can have far-reaching effects on their mental health. Studies have shown that financial stress within the family can lead to increased levels of anxiety, depression, and behavioral problems among adolescents (Conger et al., 2010).

Moreover, the economic crisis in Greece has exacerbated existing disparities in mental health care access, particularly in marginalized communities, such as especially for the vulnerable groups, uninsured, unemployed, older people, migrants, children (Lazaratou et al., 2018). This has resulted in inadequate support for vulnerable adolescents struggling with mental health issues in the wake of parental bankruptcy.

However, despite the growing body of literature on the impact of economic crises on mental health, research on the specific effects of parental bankruptcy on adolescent mental health in Greece is scarce. The current mini-review aims to fill this gap in the literature by synthesizing existing research on the topic.

Overall, this mini-review highlights the urgent need for targeted interventions and policies that address the mental health needs of adolescents affected by parental bankruptcy in the context of Greece's economic crisis.

BACKGROUND ON THE ECONOMIC CRISIS IN GREECE AND ITS IMPACT ON FAMILIES

The economic crisis that hit Greece in 2008 had severe and far-reaching consequences for the country's economy, society, and families (Kokkevi et al., 2014). The crisis was triggered by a combination of factors, including high levels of public debt, a global economic downturn, and a structural weakness in the Greek economy. The crisis had a profound impact on the country's population, with high levels of unemployment, poverty, and social inequality (Kaplanoglou et al., 2016, Andriopoulou et al., 2017).

The impact of the crisis on families was particularly severe. Many households experienced significant economic hardship, with job losses, salary cuts, and increasing financial insecurity (Stylianidis & Souliotis, 2019). Families struggled to meet their basic needs, such as housing, food, and healthcare. The crisis also had a profound impact on family dynamics, with increased stress, conflict, and tension within households (Kokkevi et al., 2014).

The impact of the crisis on families was not evenly distributed across the population. Vulnerable groups, such as low-income families, single-parent households, and households with children, were particularly affected (Matsaganis, 2013 Frasquilho et al., 2016). Moreover, the crisis had significant implications for family policy in Greece. The government introduced a range of measures to support families, including cash transfers, subsidies for housing and childcare, and employment support programs. However, these measures were often inadequate, poorly targeted, and undermined by the broader economic and political context.

In conclusion, the economic crisis in Greece had a profound and enduring impact on families, with significant implications for their economic security, social wellbeing, and family dynamics. The crisis exposed the vulnerabilities and inequalities in the Greek social and economic system and highlighted the need for targeted and effective policies to support families during times of economic hardship.

OVERVIEW OF THE RELATIONSHIP BETWEEN ECONOMIC HARDSHIP AND ADOLESCENT MENTAL HEALTH

Adolescence is a critical period for mental health development and economic hardship can have significant negative impacts on this process. Studies have shown that the crisis had a disproportionate impact on the mental health and wellbeing of children and young people, with increased rates of depression, anxiety, and behavioral problems (Economou et al., 2013; Matsaganis et al., 2015).

A study conducted by Kokkevi and her collaborators in 2018 investigate the impact of the recession on adolescents' lives in Greece and trends in well-being indicators before and during the crisis. Anonymous questionnaires were completed by stratified probability samples of 11, 13, and 15-year-old students. The results showed that students' life satisfaction has decreased, and older students reported more significant effects of the crisis than younger ones. Cannabis use increased among boys, while smoking and alcohol consumption decreased in both genders. Economic crisis was associated with more cannabis use and smoking among both genders and more alcohol consumption among boys (Kokkevi et al., 2018).

Research has shown that economic stress can lead to deterioration in children's mental health, mainly through changes in family relationships and parenting quality (Frasquilho et al., 2016; Matsaganis, 2013). In fact, adolescents who perceive themselves as being socioeconomically worse off have a four-times higher likelihood of rating low life satisfaction and quality of life (Stanojevic-Jerkovic et al., 2017). Children with unemployed parents have a higher prevalence of depression, higher rates of psychosomatic symptoms, and lower perceptions of psychological well-being (Zavras et al., 2016).

Moreover, the country's most hit by the recession have faced a rise in psychological health complaints (9-17%), which was related to the increase in unemployment rates (Frasquilho et al., 2016; OECD, 2015). A survey that takes pant Canadian adolescents' total suicide-related behavior during periods of recession illustrate that the downward trends in suicidal behavior stopped after the onset of the recession, though no increase has been reported (Rhodes et al., 2014).

DISCUSSION OF FACTORS THAT EXACERBATE THE NEGATIVE IMPACT OF PARENTAL BANKRUPTCY ON ADOLESCENT MENTAL HEALTH, SUCH AS ECONOMIC HARDSHIP, FAMILY STRESS, AND SOCIAL STIGMA

Parental bankruptcy can have a profound impact on the mental health of adolescents, as it often coincides with economic hardship, family stress, and social stigma. The consequences of parental bankruptcy haven't been extensively studied and no attention has been given to the factors that exacerbate its negative impact on adolescent mental health.

Economic Hardship

The economic crisis in Greece has led to widespread unemployment and financial hardship, particularly for families with children. The loss of income and stability can cause significant stress for parents, which can affect their ability to provide emotional support for their children. Economic hardship can also limit access to healthcare, education, and other essential resources, further compounding the impact of parental bankruptcy on adolescent mental health (Frasquilho et al., 2016; McLoyd, 1989; Ifanti et al., 2013).

Family Stress

The stress of parental bankruptcy can lead to conflict and tension within families, which can in turn negatively affect adolescent mental health. Financial difficulties may lead to arguments about money, strained relationships, and even divorce. Additionally, parents who are struggling with the emotional toll of bankruptcy may have less time and energy to devote to their children, further exacerbating the impact on adolescent mental health (Kokkevi et al., 2014; Kwon et al., 2004).

Social Stigma

Bankruptcy is often viewed as a personal failure or character flaw, which can lead to social stigma and discrimination for families experiencing financial distress. The social stigma surrounding bankruptcy can affect adolescent mental health by causing feelings of shame, isolation, and low self-esteem. Stigma can also lead to reluctance to seek help and support, which can prolong the negative impact of parental bankruptcy on adolescent mental health (Graeber, 2016; Hyman, 2012).

The negative impact of parental bankruptcy on adolescent mental health is complex and multifaceted. Economic hardship, family stress, and social stigma are all factors that can

exacerbate this impact. Mental health interventions must take into account these factors and address them in order to effectively support the mental health and well-being of adolescents experiencing parental bankruptcy in the context of the economic crisis in Greece. By reducing the stigma surrounding bankruptcy, providing resources to families in financial distress, and promoting family support and communication, we can work towards mitigating the negative impact of parental bankruptcy on adolescent mental health.

IMPLICATIONS AND FUTURE DIRECTIONS

Implications for Policy and Practice in Supporting the Mental Health of Adolescents in Greece

To mitigate the impact of the economic crisis on adolescent mental health, it is important for policymakers and practitioners to take action. One approach is to provide financial support to families who are struggling due to the economic crisis. This can include financial assistance programs for low-income families, tax breaks for households with children, and increased funding for mental health services in schools. Additionally, policymakers and practitioners can work to reduce the stigma associated with parental bankruptcy and mental illness, which can help adolescents feel more comfortable seeking help and support. These support services can be implemented through government initiatives or non-governmental organizations. Therefore, policymakers and stakeholders need to focus on developing and implementing such programs to address the mental health needs of adolescents affected by parental bankruptcy during economic crisis in Greece.

Furthermore, it is important to acknowledge that the economic crisis in Greece is not the sole factor contributing to the negative impact on adolescent mental health. Other factors, such as social and cultural norms, also play a role. Therefore, a comprehensive approach that addresses these various factors is needed to effectively support the mental health of adolescents in Greece.

Future Research Directions for Understanding the Impact of Parental Bankruptcy on Adolescent Mental Health in Different Contexts and Populations

The economic crisis in Greece has led to a significant increase in the number of households experiencing financial hardship, including bankruptcy. Previous research has shown that bankruptcy can have a negative impact on the mental health of adolescents (Wahlbeck & McDaid, 2012). However, there is still much to be learned about the mechanisms by which parental bankruptcy affects adolescent mental health, as well as the factors that exacerbate or mitigate this impact.

Factors To Consider

One area that requires further investigation is the role of social support in mitigating the negative impact of parental bankruptcy on adolescent mental health. Research has shown that social support can buffer the effects of stress on mental health (Aneshensel & Stone, 1982). However, it is unclear how social support operates in the context of parental bankruptcy. Future research could examine the types of social support that are most effective in reducing the negative impact of parental bankruptcy on adolescent mental health, as well as the factors that influence the availability and accessibility of social support for adolescents in this context.

Another area for future research is the impact of cultural factors on the relationship between parental bankruptcy and adolescent mental health. Previous research has shown that cultural factors can play an important role in shaping the experience and expression of mental health problems (Kleinman, 1988). In the context of parental bankruptcy, cultural factors such as family

values and attitudes towards financial difficulties may influence how adolescents perceive and cope with the financial stress associated with bankruptcy. Future research could explore how cultural factors interact with the impact of parental bankruptcy on adolescent mental health in different populations.

Finally, another area for future survey could explore how economic hardship, family stress and social stigma interact with each other and contribute to the overall impact of parental bankruptcy on adolescent mental health.

CONCLUSION

In conclusion, the impact of economic hardship on adolescent mental health is substantial, and policymakers need to take measures to mitigate its effects. Early intervention, family support, and mental health services are crucial to reduce the negative impact of economic hardship on adolescent mental health. The economic crisis in Greece has highlighted the need for further research into the impact of parental bankruptcy on adolescent mental health. Future research could investigate the role of social support in mitigating the negative impact of bankruptcy, as well as the influence of cultural factors on the relationship between bankruptcy and adolescent mental health. By gaining a deeper understanding of these issues, policymakers and mental health professionals can develop more effective interventions to support the mental health of adolescents in the context of economic hardship.

REFERENCES

Aneshensel, C. S., & Stone, J. D. (1982). Stress and depression: A test of the buffering model of social support. Archives of General Psychiatry, 39(12), 1392-1396.

Eirini Andriopoulou & Alexandros Karakitsios & Panos Tsakloglou, 2017. "Inequality and poverty in Greece: Changes in times of crisis," DEOS Working Papers 1705, Athens University of Economics and Business.

Conger, R. D., Conger, K. J., & Martin, M. J. (2010). Socioeconomic status, family processes, and individual development. Journal of Marriage and Family, 72(3), 685-704.

Economou, C., Kaitelidou, D., Katsikas, D., Siskou, O., & Zafiropoulou, M. (2016). Impacts of the economic crisis on access to healthcare services in Greece with a focus on the vulnerable groups of the population1. Social Cohesion and Development, 9(2), 99–115.

Economou, M., Madianos, M., Theleritis, C., Peppou, L. E., Stefanis, C. N., & Christodoulou, G. N. (2013). Suicidal ideation and reported suicide attempts in Greece during the economic crisis. World psychiatry, 12(1), 53.

Frasquilho, D., Matos, M. G., Salonna, F., Guerreiro, D., Storti, C. C., Gaspar, T., & Caldas-de-Almeida, J. M. (2016). Mental health outcomes in times of economic recession: a systematic literature review. BMC public health, 16(1), 115.

Frasquilho D, de Matos MG, Santos T, Gaspar T, Caldas de Almeida J. Unemployment as a source of mental distress to individuals and their family: Unemployed parents' perceptions during the economic recession. International Journal of Social Psychiatry. 2016;62(5):477- 48

Graeber, D. (2014). Debt-updated and expanded: The first 5,000 years. Melville House, New York.

Hyman, L. (2012). Borrow: The American way of debt. Vintage Books, New York.

Kaplanoglou G. and Rapanos V.T. (2016) "Evolutions in consumption inequality and poverty in Greece: The impact of the crisis and austerity policies", Review of Income and Wealth

Karamessini, M., & Rubery, J. (2014). Women and austerity: The economic crisis and the future for gender equality. Routledge.

Kleinman, A. (1988) Rethinking psychiatry: From cultural category to personal experience., New York Free Press.

Kokkevi, A., Stavrou, M., Kanavou, E. et al. Adolescents in Greece in Time of Economic Crisis. Child Ind Res 11, 945–962 (2018)

Kokkevi, Anna; Stavrou, Myrto; Kanavou, Eleftheria; Fotiou, Anastasios (2014). The Repercussions of the Economic Recession in Greece on Adolescents and their Families, Innocenti Working Papers, no. 2014-07

Kwon, H-K., Rueter, M. A., Lee, M-S., Koh, S., & Ok, S. W. (2004). Marital relationships following the Korean economic crisis: Applying the family stress model. Journal of Family Psychology, 17(3), 410-420.

Matsaganis, M. (2013). The Greek crisis: Social impact and policy responses. In The Great Recession and the distribution of household income (pp. 117-145). Edward Elgar Publishing.

Matsaganis, M., & Leventi, C. (2013). The distributional impact of the crisis in Greece: a microsimulation approach. Bulletin of Economic Research, 65(3), 213-231.

McLoyd, V. C. (1989). Socialization and development in a changing economy: The effects of paternal job and income loss on children. American Psychologist, 44(2), 293–302

Hyman, L. (2012). Borrow: The American way of debt. Vintage Books, New York.

Ifanti, A. A., Argyriou, A. A., Kalofonou, F. H., & Kalofonos, H. P. (2013). Financial crisis and austerity measures in Greece: Their impact on health promotion policies and public health care. Health Policy, 113(1-2), 8-12.

OECD. (2015). OECD Employment Outlook 2015. OECD Publishing.

Rhodes AE, Lu H, Skinner R. Time trends in medically serious suicide-related behaviours in boys and girls. Can J Psychiatry. 2014;59(10):556–60.

Stylianidis S, Souliotis K. The impact of the long-lasting socioeconomic crisis in Greece. BJPsych Int. 2019 Feb;16(1):16-18. doi: 10.1192/bji.2017.31. PMID: 30747163; PMCID: PMC6357520

Wahlbeck K, McDaid D. Actions to alleviate the mental health impact of the economic crisis. World Psychiatry. 2012 Oct;11(3):139-45.

Zavras D, Zavras AI, Kyriopoulos II, Kyriopoulos J. Economic crisis, austerity and unmet healthcare needs: the case of Greece. BMC Health Serv Res. 2016 Jul 27; 16:309.

Applied Sciences Research Periodicals
May 2023, Vol. 1, No. 2, pp. 11-30

The Efficacy of Two Specific Toll-Like Receptor 4 Antagonists (G2013 & M2000) In Clinical Inflammatory Disease

Mahsae Taeb[1,2], Mehdi Rahmani[2], Laleh Sharifi[3], Abbas Mirshafiey[1,4]

1. Department of Immunology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Immunology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
3. Uro-Oncology Research Center, Tehran University of Medical Sciences, Tehran, Iran
4. Livonian Biotech Millennium Ltd, Riga, LV-1013, Latvia

Abstract:
Toll-like receptors (TLRs) are receptors of the innate immune system that detect pathogen- associated molecular patterns and endogenous "danger" molecules. Among the family, the fundamental role of Toll-like receptor 4 (TLR 4) has been underscored in the initiation of pro- inflammatory cellular signaling pathways. Therefore, the appropriate suppression of Toll-like receptor 4 signaling is vital to maintain the balance between autoimmunity and inflammatory responses to avoid detrimental effects caused by the host immune system. This paper reviewed the structure of TLRs and their essential role in inflammation, specifically Toll-like receptor 4, its signaling cascade, and its antagonists. Recently, using two new drugs, M2000 (β-D-Mannuronic acid) and G2013 (α-L-Guluronic acid), the novel Toll-like receptor 4 antagonists are proposed to control inflammatory conditions. Immunosuppressive and anti-inflammatory properties of M2000 and G2013 have been examined in invitro, pre-clinical, and clinical trial studies. Experimental and clinical studies on these drugs revealed TLR4 antagonistic properties with significant efficacy for controlling inflammatory responses and treating autoimmune diseases.

Keywords: Toll-like receptor 4, Mannuronic acid, Guluronic acid, M2000, G2013, Inflammation

TOLL-LIKE RECEPTORS

The immune system consists of two closely related systems known as the innate and adaptive immune systems. While the adaptive immune system responds to specific "non-self" antigens and generates an immunological memory, the innate immune system runs an immediate first line of defense against various invading pathogens. Cognate pattern recognition receptors (PRRs), critical mechanisms of innate immunity, act as sentinels against both invading organisms bearing PAMPs [1], and damage-associated molecular patterns (DAMPs) consist of endogenous molecules released from stressed or dying cells, including hyaluronan, heat-shock proteins (HSPs) and fibronectin that promoted inflammatory pathway [2]. Toll-like Receptors are the most famous members of PRRs [3]. They are a large group of type I transmembrane proteins, of which thirteen of them have been identified in humans and mice [4], and facilitate the recognition of PAMPs or endogenous "danger" molecules [5-7]. Each TLR seems to recognize distinct PAMPs derived from various microorganisms, such as bacteria, viruses, protozoa, and fungi. Recognition of their ligands leads to the induction of signaling events and results in acute host responses that eventually causes pathogens' death [8, 9].

Thirteen recognized TLRs could sense a wide variety of pathogen structures, including triacyl lipopeptides by TLR1 in association with TLR2, lipoteichoic acid and lipoproteins of Gram-positive

bacteria by TLR2, double- stranded RNA by TLR3, LPS of Gram-negative bacteria by TLR4, bacterial flagellin by TLR5, diacyl lipopeptides by TLR6 in association with TLR2, single-stranded RNA by TLR7 and nonmethylated CpG of bacterial DNA by TLR9 [8].

Among these identified types, humans express ten functional TLRs (TLR1 to TLR10), whereas twelve TLRs (TLR1 to TLR9 and TLR11 to TLR13) exist in mice. Human TLR10, mouse TLR12, and mouse TLR13 are the only types whose ligands have not been identified yet [9].

Cell locations divided TLRs into two groups. The first group includes TLR1, TLR2, TLR4, TLR5, and TLR6, which are located on the cell surface, and the second one comprises TLR3, TLR7, TLR8, TLR9, TLR11, TLR12, and TLR13 that are within endosomes, endoplasmic reticulum (ER), multivesicular bodies, and lysosomes [10]. This localization prevents autoimmunity and inappropriate immune responses [11, 12].

Generally, TLRs are expressed broadly in tissues and different cells, both immune and non-immune ones. Cytokines or pro-inflammatory mediators are produced after TLRs stimulation in these cells [10, 13, 14].

TLRs are glycoproteins that consist of 3 domains: a transmembrane domain, an amino-terminal ectodomain, and a cytoplasmic carboxy-terminal Toll IL1-1R homology (TIR) domain [15, 16]. The TIR domain is the part that identifies explicitly microbial components and, as a final point, triggers the activation factors that cause the production of pro-inflammatory cytokines [17]. TLR1, TLR2, TLR4, and TLR6 recruit TIR domain-containing adaptor protein (TIRAP), which serves as an adaptor between the TIR domain of TLRs and myeloid differentiation factor 88 (MyD88), while TLR5, TLR7, TLR9, and TLR11 can recruit MyD88 directly. The binding of TLR3 and TLR4 ligands results in the recruitment of Toll/IL-1R domain-containing adaptor, inducing IFN-β (TRIF). However, the recruitment of TRIF by TLR4 needs the participation of a TRIF-related adaptor molecule (TRAM) [1].

In the inflammation process, an increase in a multitude of pro-inflammatory proteins requires signal transduction processes by activated TLRs, including Nuclear Factor-κB (NF-κB) and 2 Mitogen-activated protein (MAP) kinases, p38, and Jun N-terminal kinase (JNK) [5].

Receptor-proximal proteins involved in signaling by all TLRs include the adapter MyD88, Interleukin-1 receptor- associated kinase 1 (IRAK-4, IRAK, and IRAK-2), Toll interacting protein (Tollip), TNF-receptor-associated factor 6 (TRAF-6), and transforming growth factorβ-activated kinase 1 (TAK-1) [18, 19].

TLRs family triggers inflammation by two pathways: a canonical pathway using MyD88 adaptor protein (MyD88- dependent) and a non-canonical pathway using TRIF adaptor protein (MyD88-independent). Excluding TLR3, the canonical pathway activates MAPK and NF-κB, leading to the secretion of inflammatory cytokines such as Interleukin-6 (IL-6) and Tumor Necrosis Factor α (TNF-α). On the other hand, the non-canonical pathway motivates Interferon Regulatory Factor 3 (IRF3) due to interferon production [20].

The development of cancers and inflammatory diseases, such as neuro-inflammation, autoimmune and cardiovascular diseases, may occur due to TLRs activation and excessive

activation of inflammatory pathways [21-23]. Interestingly, TLRs play anti-tumor or tumor-developing roles in different cancer cells [24]. Furthermore,

it has been suggested that unsuitable TLR recognition and signaling pathways play a role in the pathogenesis of several human age-related diseases [25].

It is well-known that TLRs, especially TLR2 and TLR4, are involved in various autoimmune and inflammatory disorders. Such as Multiple Sclerosis (MS), Ankylosing Spondylitis (AS), Rheumatoid Arthritis (RA), Type 1 Diabetes (TID), Systemic Lupus Erythematosus (SLE), and as well as Inflammatory Bowel Disease (IBD) [19]. Given the wide-ranging impact of TLRs on innate and adaptive immunity in several disease settings, their signaling pathways arise as attractive therapeutic targets [1].

TOLL-LIKE RECEPTOR 4

Toll-like receptor 4 (TLR4) is considered one of the best-understood members of the TLRs family, who identified as the first human homolog of the Drosophila Toll gene [26], first reported by Janeway's group [27, 28]. In 1998, TLR4 was recognized as the signaling receptor for LPS or endotoxin from the outer membrane of Gram-negative bacteria [29].

Human TLR-4 is located on chromosome 9q32–q33 and contains four exons [30]. Hematopoietic and non- hematopoietic cells, including endothelial cells [31], cardiac myocytes [32], and cells of the central nervous system (CNS), express TLR4 on their surface [33]. TLR4 is located on the plasma membrane and can also be an intracellular TLR since it can be internalized and stimulate intracellular pathways [34].

The exogenous PAMPs, like LPS, taxol, viral glycoproteins, rSV fusion protein, and mice mammary tumor virus (MMTV) envelope protein, are ligands that TLR4 can recognize. Besides, necrotic cells, HSPs, high mobility group box 1 (HMGB1), fibronectin, extracellular cell matrix (ECM) components, fatty acid, minimally oxidized low-density lipoprotein (mmLDL), hyaluronic acid, β-defensin-2, amyloid peptide, and fibrinogen are endogenous ligands of TLR4 [19, 26, 35]. Recently, TLR-4 was the first identified TLR whose crystal structure was solved and led to the prediction of the mechanism of its interaction with its cognate ligands [36]. Like the rest of the family, its structure consists of three domains [26]. The extracellular Leucine Reach Repeat (LRR) domain is involved in recognition of the LPS of Gram-negative bacteria. The prototypic TLR4 ligand, the foremost ligand of TLR4, is LPS and is the main factor of the outer membrane of Gram-negative bacteria [26, 36]. The TIR domain has homology with the IL-1 receptor (IL-1R), which is responsible for the propagation of the signal within the cell [36].

TLR4 signaling can follow two different intracellular pathways. From the plasma membrane, in other words, the MyD88-dependent pathway via TIRAP induces the NF-κB and activator protein-1 (AP-1), resulting in the release of inflammatory cytokines, e.g., IL-6 and TNF-α. Alternatively, from the endosome, or the MyD88-independent pathway via TLR4 initiates the TRAM-TRIF pathway, leading to the activation of IRF3, the production of type I Interferon (IFNs), and a late wave of NF-κB activation [34, 37]. Indeed, these pathways must regulate the balance between cell survival and inflammation. TLR4 activation can induce one or more of four adaptor proteins: MyD88, TICAM1 (also known as TIR domain-containing adapter molecule 1), TIRAP, and TICAM2 [38].

Activation of TLR4 requires dimerization, which happens by molecules such as Cluster of differentiation 14 (CD14) and myeloid differentiation factor-2 (MD-2) [32]. After activation through dimerization, an internal cell cascade activates, which leads to the release of several interleukins, interferons, and other signaling substances. These signals attract macrophages, NK cells, and mast cells, which subsequently may release reactive oxygen species (ROS) and reactive nitrogen species (RNS) [39].

Activating TLR4 by LPS is a complex process in that many molecules are involved, including LPS, CD14, MD2, and LPS-binding protein (LBP) [39]. LPS is composed of lipids and carbohydrates, with a high level of structural complexity, and consists of 3 different constituents that are the O antigen, an O-polysaccharide chain of variable length; the core oligosaccharide; and lipid A, which contributes to most of the immune-stimulatory activity of the molecule [11, 26, 35, 36]. Recently, It revealed that both plasma-membrane and endosome pathways of TLR4 are required to respond to LPS fully. Additionally, TLR4 intracellular signaling boosts micropinocytosis and antigen presentation, and recently, it has also been shown to be involved in the recognition and uptake of apoptotic cells [40].

Available evidence has indicated the activation or suppression of TLR4 in the development and progression of various inflammatory diseases. Hence, TLR4 can be an excellent therapeutic target for treating inflammatory diseases [29].

Three different approaches are available for pharmacological interventions in the TLR4 signal pathway: 1- anti- LPS strategies that aim to neutralize LPS; 2- TLR4 antagonism, including the MyD88 signaling pathway; and 3- targeting inflammation and ROS/RNS [39].

MYD88

MyD88 is the most significant adaptor protein for TLR4 signaling known to hyper-activate NF-κB, MAPK, and phosphoinositide 3-kinase (PI3K) pathways driving tumor survival [41].

MyD88-mediated signaling generally occurs at the plasma membrane and involves a rapid presence of MyD88 and MAL proteins. Engagement of these adaptor molecules stimulates a range of events by phosphorylation of IRAKs, the association of TRAF6, and the downstream activation of TAK1, moderated by the adaptor proteins, TAK1-binding protein 2 and TAK1-binding protein 3 (TAB2 and TAB3). TAK1, in turn, activates the MAPKs, JNK, extracellular signal-regulated kinases (ERK1/2), p38, and the IkB kinase complex (IKK), causing the activation of imperative transcription factors, such as NF-κB and AP-1, that eventually encourage the production of pro-inflammatory cytokines [6, 42]. MyD88 and TIRAP are involved in the early activation of NF-κB and MAPK, whereas TRIF and TRAM are critical for the late activation of NF-κB and the activation of IRF-3 [43]. Noulin et al. [44] analyzed the role of TLR signaling and the impact of different cell types in response to aerogenic LPS. To illustrate this, macrophages from MyD88−/− mice are inefficient in many TLR4-mediated reactions, such as LPS-induced secretion of cytokines (e.g., IL-6, TNF-α, and IL-1β), which shows the importance of MyD88 in TLR4-mediated signaling [5].

Based on recent observations, upon TLR4 activation, TIRAP facilitates the interaction of MyD88 with TLR4 via its TIR domain, and that's where the "myddosome" formed, a giant molecular platform composed of MyD88, TIRAP, and IRAK proteins [45].

Despite the differences between MyD88-dependent and MyD88-independent pathways, both contribute to host defense and involve the immune response [46]. To illustrate, in TLR4 signaling, the MyD88-dependent way is essential for cytokine induction, such as NF-κB activation. On the contrary, the MyD88- independent pathway can lead to DC maturation [27].

Since MyD88 is involved in TLR4 signaling, it plays a significant role in infectious diseases, cancer, and autoimmune diseases, so that it can be an attractive target for intervention in these diseases [1].

TLR4 AND INFLAMMATORY DISEASES

Much evidence has shown that the activation of TLR4 results in inflammation and carcinogenesis, such as gastric cancer and human epithelial ovarian cancer [1].

The functional role of Toll-like receptors, mainly TLR4, has been proposed in diseases such as atherosclerosis [47], RA [48], allergy [49], neuropathic pain [50], ischemia/reperfusion injury [51], hemorrhagic shock [52], alcohol-induced neuroinflammation [53], and diabetes [54], asthma, cardiovascular disorder, obesity, metabolic syndrome, autoimmune disorders, schizophrenia, bipolar disorder, autism, clinical depression, chronic fatigue syndrome, and toluene inhalation [39]. The roles of TLR2 and TLR4 in psoriasis, an immune-mediated skin disease characterized by abnormal keratinocyte differentiation and proliferation, are implied by increased expression of TLR2 and TLR4 on BPMCs and keratinocytes in patients [55].

Accordingly, the expression level of TLR2 and TLR4 increased in chronic inflammatory diseases of the CNS with an autoimmune origin, such as MS and its animal model, rodent experimental autoimmune encephalomyelitis (EAE) [56].

Recent studies demonstrated that TLR2/4 could be used as an interface between innate immunity and the pro- inflammatory state of Type 1 Diabetes (T1D) because the mRNA expressional levels of TLR2, TLR4, and MyD88, as well as ligands of TLR2/ TLR4, such as Hsp60 and HMGB1, are elevated in T1D patients [57].

A significant increase in expression of the TLR4 gene was shown in Peripheral Blood Mononuclear Cells (PBMCs) of AS patients compared to healthy controls [58]. In an experimental model, Kuang et al. [59] reported that TLR4 is expressed in murine tumor cells and that the activation of TLR4 in these cells by LPS induced the expression of various factors, including IL-6. Furthermore, it has been shown that the damage to the liver through alcohol consumption can be stopped by the suppression of MyD88, a molecule involved in TLR signaling [60].

TLR4 signaling, via activation of the adaptive immune reaction, could be helpful in the chemo, and radiotherapy of cancers, as TLR4-deficient animals have shown to have an inadequate response to such therapy [61].

The activation of TLR4 signaling pathways is associated with "stress-inflammation-depression." TLR4 signaling pathway may be a possible target for the anti-inflammatory treatment of depression [62].

Recently, the link between TLR and experimental autoimmune diseases, like RA, has also become apparent. It reported that inhibition of TLR4 suppressed the severity of experimental arthritis and resulted in lower IL-1 expression in arthritic joints [63].

TLR4 ANTAGONISTS

As mentioned earlier, the proper suppression of TLR-4 signaling pathways is critical to maintaining the balance between host-defense functions and inhibition of harmful effects in autoimmune [58] and chronic inflammatory disorders [64, 65], and some negative regulators control this repression to prevent aberrant inflammatory responses [66-69].

Therapeutically, some TLR antagonists (small molecules) bind selectively to TLRs and inhibit their signal transduction and downstream signaling events in different ways. Such as neutralizing antibodies to TLR ectodomains, small molecules that block enzymes in the signaling pathway (e.g., IRAK4), and finally, agents that block protein-protein interactions in the TLR signaling cascade [58, 64].

Unfortunately, the clinical use of TLR inhibitors is limited due to the need for their available ingredients [70]. Exploring new molecules that can interfere with TLRs, their co-receptors, and their signal transduction is imperative.

One of the exogenous synthetic antagonists for TLR4 is TAK-242 (Resatorvid), a Small Molecule Inhibitor (SMIs) with an anti-sepsis effect that inhibits the communication between TLR4 and two adaptor proteins (TIRAP and TRAM), which was reported to inhibit the TLR4 signal transduction and subsequently reduce the complication in different studies [29, 58].

Other SMIs are previously developed drugs, while their suppressing effect on TLR2 and TLR4 has been recently discovered, like statins and Angiotensin II Receptor Blockers (ARBs). For instance, valsartan (a member of the ARB family) can reduce the secretion of pro-inflammatory cytokines release, while vandesartan, another member of this family, can suppress both TLR2 and TLR4 activation [71-73].

Tollip, an inhibitory protein in TLR2 and TLR4 signaling pathways, is associated with IRAK-1 to reduce IRAK- 1 auto-phosphorylation levels and inhibit its kinase activity [74, 75].

ST2825, a heptapeptide analog specifically designed to inhibit MyD88 dimerization, was reported by Loiarro et al. [76]. Also, it is specific for the homo-dimerization of the TIR domains but does not affect the homo- dimerization of the death domains [77].

Since lipid A of LPS is an excellent therapeutic target for modulating the TLR4 signaling pathway, analogs of lipid A are considered TLR antagonists. For example, Eritoran (E5564) is a synthetic lipid A analog of Rhodobacter sphaeroides, which competitively binds to the MD2 and inhibits the TLR4 signaling [32].

MiR-146a has been found to inhibit the translation of the TRAF6 and IRAK1 in the downstream signaling cascade of TLR4. It has also shown that miR-146a plays a central role as an intrinsic brake on inflammation [78, 79].

Nano-inhibitors are favorable and potent TLR inhibitors, interfering with the TLR4 signaling pathway. Lipid- modified Non-Anticoagulant Heparin Nanoparticle (NAHNP) is an intriguing self-assembling nanodevice that binds to TLR4/MD2 and prevents MyD88-dependent NF-κB pathway, has an inhibitory effect on chronic inflammation in an animal model of RA [80].

Slivka et al. introduced MD-I (a minor peptide antagonist of TLR4 signaling) linked to TLR4 and can block the interaction between TLR4 and MD2 [81].

1A6 is another monoclonal antibody interfering with MD2, a co-receptor for TLR4 activation [82]. NI-0101 is a promising anti-TLR4 antibody that acts by inhibiting TLR4 dimerization, but its function is not associated with the ligand's kind or concentration [83].

Given the fact that authentic antagonists for TLR4 are very limited, M2000 and G2013 have been identified as effective drugs in the clinical phase and besides being able to control inflammation responses.

MANNURONIC ACID

Structure and Mechanism

M2000 (β-D-Mannuronic Acid) has a low molecular weight and novel patented drug (with Patent No. of DE/102016113018.4 - PCT/EP2017/067919) (Fig. 1), with no toxicity for bone marrow, liver, and kidney. This drug has been introduced as a new NSAID with immunosuppressive and anti-inflammatory properties [70], which have been confirmed in EAE, nephritic syndrome, immune complex glomerulonephritis (ICG) and adjuvant- induced arthritis (AIA) [84-87].

M2000 is one of the Alginic acid comonomers extracted from alginate by the chemical hydrolysis method in the Immunology Department of Tehran University of Medical Sciences [70, 84].

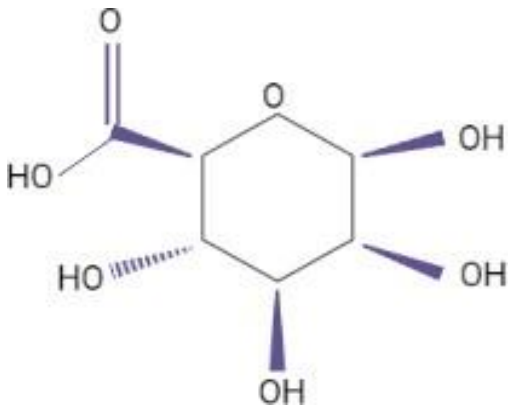


Figure 1. The chemical structure of M2000 (b-D-mannuronic acid) patented (DE-102016113018.4)

M2000, as a novel NSAID with antidiabetic, cardioprotective, and anti-tumoral efficacy, has shown excessive tolerability and safety profile with no or mild adverse events compared with many other medicines in treating different experimental and in vitro diseases [88].

As previously mentioned, due to the importance of TLRs in the pathogenesis of inflammatory disorders, inhibiting TLRs signals can be beneficial in treating such diseases [89]. Generally, because of the structure and immunostimulatory activity of alginate oligomers of M2000, this drug can act as a carbohydrate antagonist for TLR2 and 4 [90].

In Vitro And Experimental Studies

M2000, as a novel NSAID, has immunosuppressive effects on autoimmune diseases such as myelodysplastic syndrome (MDS). Treated-PBMCs by this drug showed a significant reduction of IL-6 and TNF-α as inflammatory cytokines and a significant increase in the level of Granulocyte colony-stimulating factor (G-CSF) gene expression [91].

Our previous study indicated that the activity of the cyclooxygenase 1 (COX-1) and cyclooxygenase 2 (COX-2) enzymes as primary factors in the progression of inflammatory and autoimmune diseases was strongly inhibited by M2000 [92].

In 2019 in another research, we showed that M2000 could modify oxidative stress by lowering expression levels of the Super Oxide Dismutase 2 (SOD2), Glutathione S-transferase (GST), Inducible nitric oxide synthase (iNOS), and myeloperoxidase (MPO) genes compared to the healthy expression levels, with a probable reduction of the risk of developing inflammatory diseases related to age and aging [93].

In connection with the inhibitory effect of M2000, Sharifi et al. showed that M2000 could suppress the TLR2 and TLR4 mRNA expression in HT29 cell lines. Since HT29 cells are human colon adenocarcinoma cell lines and are always used as a model of luminal surface colonic epithelial cells in vitro, It's hypothesized that this drug can reduce inflammatory responses and oxidative stress in IBD patients [94].

In 2017, Aletaha et al. showed efficient inhibition of MyD88, NF-κB, TNF-α, and IL-6 expression in HEK293 cell lines [90], and also Mortazavi Jahromi et al. at the same period showed that M2000 could modify TLR2 signaling through inhibition of the adapter molecules IRAK1 and TRAF6, the transcription factor NF-κB, miR- 146a and finally the reduction of pro-inflammatory cytokines production [95].

Tolerability and anti-inflammatory effects of M2000 have been established when administered orally in animals in various models of EAE, AIA, nephrotic syndrome, and acute glomerulonephritis [85, 96-98]. In support of this, Fattahi et al., in their preclinical study, not only found no mortality and no abnormality in clinical signs, body weight, relative organ weights, necropsy, and no significant difference in hematological, biochemical, and histopathological parameters in any of the animals in experimental models [98, 99] but also indicate that the optimum dosage of this drug, could be considered almost safe for humans [87].

According to the studies, the immunosuppressive effects of M2000 were found in animal models and cell lines [85, 100]; Also, the anti-oxidant property of M2000 and its monomer G2013 was proven in animal models [101- 103]. In the M2000-treated diabetic rats, it was found that serum glucose levels were decreased, followed by an increase in serum insulin levels. Also, a dramatic reduction in the inflammatory markers and also symptoms were seen [104].

The study on microRNAs (miRNAs) in Type 2 diabetes mellitus (T2DM) rats showed upregulating in the expression level of miR-34a in rats treated with M2000. In the same way, a dramatic decrease in expression levels of miR-126 and miR-125a-5p has been observed in those rats after treatment with β-D mannuronic acid and α-L- guluronic acid, respectively [105]. These miRNAs, especially in higher expression, are considered potential biomarkers for T2D diagnosis [106, 107].

Clinical Studies

Following the observation of the positive effects of M2000 in an animal breast cancer model [108], a clinical trial of phase II breast cancer patients found a reduction in gene expression which plays a notable role in the development of chronic inflammation, angiogenesis, tumorigenesis, and metastasis including, MMP-2, MMP-9, CCL22 and TGFβ1, and Regulatory T Cells (Tregs) frequency [109].

Accordingly, the efficacy and safety of M2000 were approved in clinical trial Phase I/II on RA. This drug has shown an inhibitory effect on Anti-Cyclic Citrullinated Peptide Antibodies (anti-CCP), Rheumatoid Factor (RF), anti-double strand DNA (anti-dsDNA), acute phase reactants, and also a reduction in IL17 and Retinoic acid- related orphan receptor γ t (RORγt) gene expression after oral administration in RA patients [110].

Oral administration of M2000 in phase III RA patients showed a reduction in the expression of miR-155 and NF- κB as long as to increase the expression of suppressor of cytokine signaling-1 (SOCS1) and SH2 domain- containing inositol-5′-phosphatase 1 (SHIP1) in treated- PBMCs in these patients [87].

The β-D-mannuronic acid significantly reduced the disease activity and physical function of patients with AS. Also, the gene expression of Myd88, IKBalpha, and NF-κB was downregulated by inhibiting the TLR/ NF-κB Signaling Pathway in these patients after treatment [58].

In 2018, Fattahi et al., in a clinical trial study, showed the effect of M2000 on inflammatory responses in phase I/ II AS patients was more impressive than naproxen and placebo. And also, the incidence of gastrointestinal and other side effects was less in patients treated with M2000 [111].

In the most recent clinical trial on patients with secondary progressive MS, Najafi et al. have shown that M2000 can downregulate IL-17, STAT1, and STAT3 genes in addition to reducing the expression of TLR2 and TLR4 on PBMCs [112].

GULURONIC ACID

Structure and Mechanism

The α-L-guluronic acid (G2013) [113] with the molecular formula ($C_6H_{10}O_7$) is a monomer of M2000, prepared from alginic acid sodium salt (Fig. 2), has advantages including its low molecular weight and natural base, immunomodulatory and anti-aging effects along with high safety property [103, 114-116].

This drug was discovered after M2000, and the purification method was carried out based on a modified procedure of the acid hydrolysis method by Nazeri et al. [114].

G2013, as an NSAID, is a novel immunosuppressive agent with no or little side effect in increasing the risk of infectious diseases and cancers [117].

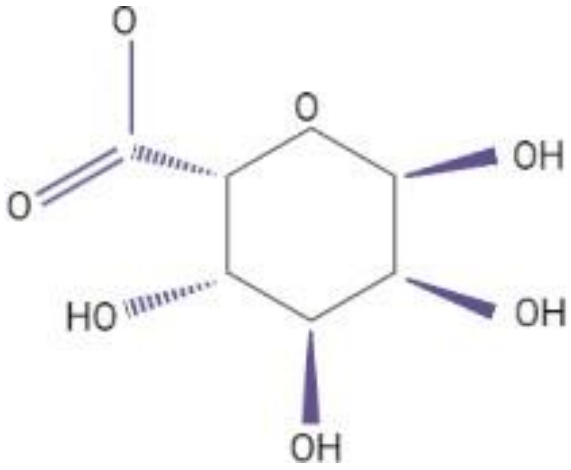


Figure 2. The chemical structure of G2013 (α-L-guluronic acid) patented (PCTEP2017067920)

In Vitro And Experimental Studies

In 2018, the researchers found that although G2013 had no profound impact on the protein expression of TLR2 and TLR4, it had an immunomodulatory effect on the TLR2 and TLR4 signaling cascade (e.g., NF-κB, IκB, and MyD88) and cytokine production by PBMCs like IL-1β [118]. It is also specified that G2013 not only can moderate the TLR4 signaling pathway by decreasing downstream signaling molecules but also has no effect on miR-146a gene expression as an anti-inflammatory factor in innate immunity (Fig. 3) [119].

Sharifi et al. in 2018 showed that G2013 significantly reduces NF-κB, IkB, and MyD88 mRNA expression and also decreases the secretion of IL-1β in human mononuclear cells [118].

Our previous study on the anti-aging and anti-inflammatory effects of the G2013 (guluronic acid) showed that this drug, as well as M2000, can reduce the genes expression of several oxidative stress (e.g., iNOS) [116], and also COX-1 and COX-2 enzymes in PBMCs [120].

A study in G2013 showed that this drug's anti-inflammatory and immunomodulatory effects lead to the induction of SHIP1, SOCS1 and reduce TLR4, MyD88, and NF-κB at the level of gene expression and decrease IL-1β as a pro-inflammatory cytokine in HEK-Blue hTLR4 cell line [4].

According to the other studies G2013, as well as M2000, can significantly reduce the Mean Fluorescence Intensity (MFI) of TLR2 and TLR4 as well as gene expression of NF-κB in Common Variable Immunodeficiency (CVID) [70, 102, 121, 122].

Subsequently, another study in 2019 revealed a significant downregulating in TLR2 and TLR4 gene expression in HT29 cell lines treated by G2013, which can exert its inhibitory effect [100].

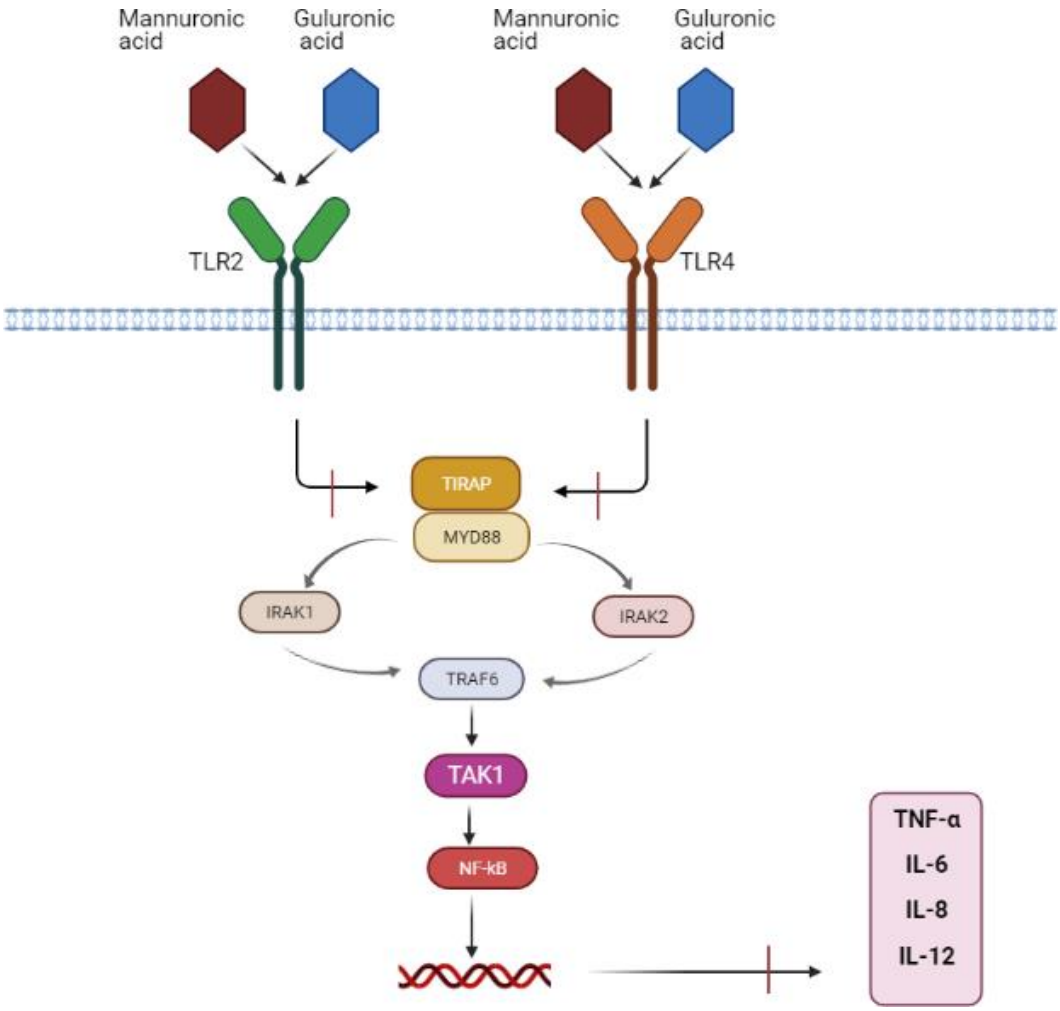


Figure 3. The β-D-Mannuronic Acid and α-L-Guluronic acid are able to affect the inflammatory pathways associated with TLR4 (and also TLR2), and consequently the reduction of inflammatory factors

Afraei et al. analyzed the model of EAE and showed that all signs of inflammation (such as serum nitric oxide (NO) levels in G2013- treated mice, were less than in the control group [123].

G2013, a potent inflammatory agent with potential anti-tumor activity, indicated that it could quickly reduce cancer-related inflammation without direct toxic effects on the cells in a murine breast cancer model [124].

PBMCs extracted from MS patients showed a decrease in the expression level of TLR2, TLR4, and TLR-α genes after being treated by G2013 [125].

Clinical Studies

The combination of G2013 with current therapy in conventional-treated RA patients has shown a positive effect, and its safety, efficacy, and tolerability are well-illustrated [126]. During a clinical study on RA patients, receiving oral administration of G2013 showed a significant increase in IL-4 and GATA-3 and a considerable decrease in RORγt gene expression after 12 weeks of treatment [127].

The investigation has shown that G2013 had a dual effect on pro-inflammatory cytokines and their transcription factors in phase I/II of RA patients. In this clinical study, a significant decrease in the level of IFNγ and Aryl Hydrocarbon Receptor (AHR) and a significant induction in gene expression of IL10 and Forkhead box P3 (FOX- P3) were seen [128].

In 2019, the study showed that oral administration of G2013 to AS patients reduced the expression levels of the RORγt, IL-17, AHR, and IL-22 and increased the gene expression levels of the GATA3, IL-4, and FOXP3. This drug can also modify the severity of articular and inflammatory signs in these patients [129].

Nazeri et al. showed that G2013 had the same effect as naproxen on AS patients and had more notable safety characteristics in identifying information than that drug [130].

Since G2013 as well as M2000, is an immunomodulatory agent which inhibits TLRs signaling, it could be considered a therapeutic target in inflammatory diseases [94].

CONCLUSION

TLRs, as an essential member of the innate immune system, recognize PAMPs and DAMPs following the activation of their signaling and triggering the inflammatory responses [1, 90].

TLR activation induces the expression of hundreds of genes, including inflammatory cytokines, chemokines, antimicrobial proteins and peptides, tissue repair, coagulation factors, and metabolic regulators. According to these facts, TLR signaling inhibition can be essential to the inflammation suppression process. TLR4, due to its close relation with inflammatory diseases, can be one of the best possible therapeutic targets in cancers and inflammatory diseases.

Since all TLR4 antagonists have acted in the preclinical phase so far, this review aims to evaluate the antagonistic, anti-inflammatory, and immunosuppressive effects of M2000 and G2013 as the only clinical antagonists on the TLR4 function. Many studies assessed whether the anti-inflammatory properties of these drugs affect the inflammation signal pathway in humans. M2000 and G2013 have been tested several times as anti-inflammatory and novel immunosuppressive agents in various experimental and clinical models [58, 70, 84, 87, 92, 94, 98, 99, 130-134].

Research has shown that the moderating effect of these novel NSAIDs can affect the inflammatory pathways associated with TLR4 (and also TLR2) and consequently reduce inflammation [4, 58, 90, 102, 118, 122].

Accordingly, M2000 and its monomer, G2013, not only prevent the progression of inflammation and reduce symptoms associated with TLR4 in experimental models of MS, AIA, nephrotic syndrome, acute glomerulonephritis, T2DM, animal Breast Cancer, and diabetic rats [85, 88, 96-99, 104, 105, 108, 118, 123] but also in clinical phase including phase I/II AS patients [58, 111, 129, 130] phase I/ II/ III in RA patients [87, 110, 126-128] in human BC [109, 124] as well as in MS patients under in vitro conditions [125] have shown positive results. These drugs cause a reduction of pro-inflammatory cytokines production related to TLR signaling and modify TLRs signaling in some cell lines by a new therapeutic approach [94, 95, 122].

Studies on these new drugs may provide important insight into the nature of the inflammatory responses and lead to the development of novel treatments for inflammatory diseases.

Declarations

- Ethics approval and consent to participate: Not applicable

REFERENCES

1. Zhu, J. and C. Mohan, Toll-like receptor signaling pathways—therapeutic opportunities. Mediators of inflammation, 2010. 2010.
2. Pandolfi, F., et al., Key role of DAMP in inflammation, cancer, and tissue repair. Clinical therapeutics, 2016. 38(5): p. 1017-1028.
3. Barton, G.M. and J.C. Kagan, A cell biological view of Toll-like receptor function: regulation through compartmentalization. Nature Reviews Immunology, 2009. 9(8): p. 535-542.
4. Mortazavi-Jahromi, S.S., et al., Effects of guluronic acid (G2013) on SHIP1, SOCS1 induction and related molecules in TLR4 signaling pathway. International Immunopharmacology, 2018. 55: p. 323- 329.
5. Laird, M.H., et al., TLR4/MyD88/PI3K interactions regulate TLR4 signaling. Journal of leukocyte biology, 2009. 85(6): p. 966-977.
6. Chen, C.-Y., C.-L. Kao, and C.-M. Liu, The cancer prevention, anti-inflammatory and anti-oxidation of bioactive phytochemicals targeting the TLR4 signaling pathway. International journal of molecular sciences, 2018. 19(9): p. 2729.
7. Wu, Y.-w., W. Tang, and J.-p. Zuo, Toll-like receptors: potential targets for lupus treatment. Acta Pharmacologica Sinica, 2015. 36(12): p. 1395-1407.
8. Calich, V.L., et al., Toll-like receptors and fungal infections: the role of TLR2, TLR4 and MyD88 in paracoccidioidomycosis. FEMS Immunology & Medical Microbiology, 2008. 53(1): p. 1-7.
9. Lee, C.C., A.M. Avalos, and H.L. Ploegh, Accessory molecules for Toll-like receptors and their function. Nature Reviews Immunology, 2012. 12(3): p. 168-179.
10. McClure, R. and P. Massari, TLR-dependent human mucosal epithelial cell responses to microbial pathogens. Frontiers in immunology, 2014. 5: p. 386.
11. Marongiu, L., et al., Below the surface: The inner lives of TLR4 and TLR9. Journal of leukocyte biology, 2019. 106(1): p. 147-160.
12. Akira, S., S. Uematsu, and O. Takeuchi, Pathogen recognition and innate immunity. Cell, 2006. 124(4): p. 783-801.
13. Lavelle, E.C., et al., The role of TLRs, NLRs, and RLRs in mucosal innate immunity and homeostasis. Mucosal immunology, 2010. 3(1): p. 17-28.
14. Kawai, T. and S. Akira, The roles of TLRs, RLRs and NLRs in pathogen recognition. International immunology, 2009. 21(4): p. 317-337.
15. Bell, J.K., et al., Leucine-rich repeats and pathogen recognition in Toll-like receptors. Trends in immunology, 2003. 24(10): p. 528-533.
16. O'Neill, L.A. and A.G. Bowie, The family of five: TIR-domain-containing adaptors in Toll-like receptor signalling. Nature Reviews Immunology, 2007. 7(5): p. 353-364.

17. Hosseini, A.M., et al., Toll-like receptors in the pathogenesis of autoimmune diseases. Advanced pharmaceutical bulletin, 2015. 5(Suppl 1): p. 605.

18. O'Neill, L.A., et al., Mal and MyD88: adapter proteins involved in signal transduction by Toll-like receptors. Journal of endotoxin research, 2003. 9(1): p. 55-59.

19. Liu, Y., et al., TLR2 and TLR4 in autoimmune diseases: a comprehensive review. Clinical reviews in allergy & immunology, 2014. 47(2): p. 136-147.

20. Kawasaki, T. and T. Kawai, Toll-like receptor signaling pathways. Frontiers in immunology, 2014. 5: p. 461.

21. Wu, K., et al., TLR4/MyD88 signaling determines the metastatic potential of breast cancer cells. Molecular medicine reports, 2018. 18(3): p. 3411-3420.

22. Wang, L., et al., Dual functional roles of the MyD88 signaling in colorectal cancer development. Biomedicine & Pharmacotherapy, 2018. 107: p. 177-184.

23. Johnson, R.H., et al., The functional and inflammatory response of brain endothelial cells to toll-like receptor agonists. Scientific reports, 2018. 8(1): p. 1-12.

24. Dajon, M., K. Iribarren, and I. Cremer, Toll-like receptor stimulation in cancer: a pro-and anti-tumor double-edged sword. Immunobiology, 2017. 222(1): p. 89-100.

25. Balistreri, C.R., et al., Role of TLR polymorphisms in immunosenescence, in Handbook on Immunosenescence. 2009, Springer. p. 659-671.

26. Balistreri, C.R., et al., TLR4 polymorphisms and ageing: implications for the pathophysiology of age-related diseases. Journal of clinical immunology, 2009. 29(4): p. 406-415.

27. Kaisho, T. and S. Akira, Dendritic-cell function in Toll-like receptor-and MyD88-knockout mice. Trends in immunology, 2001. 22(2): p. 78-83.

28. Medzhitov, R., P. Preston-Hurlburt, and C.A. Janeway, A human homologue of the Drosophila Toll protein signals activation of adaptive immunity. Nature, 1997. 388(6640): p. 394-397.

29. Matsunaga, N., et al., TAK-242 (resatorvid), a small-molecule inhibitor of Toll-like receptor (TLR) 4 signaling, binds selectively to TLR4 and interferes with interactions between TLR4 and its adaptor molecules. Molecular pharmacology, 2011. 79(1): p. 34-41.

30. Opal, S.M. and C.T. Esmon, Bench-to-bedside review: functional relationships between coagulation and the innate immune response and their respective roles in the pathogenesis of sepsis. Critical Care, 2002. 7(1): p. 23.

31. Jenkins, K.A. and A. Mansell, TIR-containing adaptors in Toll-like receptor signalling. Cytokine, 2010. 49(3): p. 237-244.

32. Park, B.S., et al., The structural basis of lipopolysaccharide recognition by the TLR4–MD-2 complex. Nature, 2009. 458(7242): p. 1191-1195.

33. Molteni, M., S. Gemma, and C. Rossetti, The role of toll-like receptor 4 in infectious and noninfectious inflammation. Mediators of inflammation, 2016. 2016.

34. Kagan, J.C., et al., TRAM couples endocytosis of Toll-like receptor 4 to the induction of interferon-β. Nature immunology, 2008. 9(4): p. 361-368.

35. Kuzmich, N.N., et al., TLR4 signaling pathway modulators as potential therapeutics in inflammation and

sepsis. Vaccines, 2017. 5(4): p. 34.

36. Mai, C.W., Y.B. Kang, and M.R. Pichika, should a Toll-like receptor 4 (TLR-4) agonist or antagonist be designed to treat cancer? TLR-4: its expression and effects in the ten most common cancers. OncoTargets and therapy, 2013. 6: p. 1573.

37. Dauphinee, S.M. and A. Karsan, Lipopolysaccharide signaling in endothelial cells. Laboratory investigation, 2006. 86(1): p. 9-22.

38. Kumar, V., Innate lymphoid cells: new paradigm in immunology of inflammation. Immunology letters, 2014. 157(1-2): p. 23-37.

39. Lucas, K. and M. Maes, Role of the Toll Like receptor (TLR) radical cycle in chronic inflammation: possible treatments targeting the TLR4 pathway. Molecular neurobiology, 2013. 48(1): p. 190-204.

40. Thomas, L., et al., The N-terminus of CD14 acts to bind apoptotic cells and confers rapid-tethering capabilities on non-myeloid cells. PLoS One, 2013. 8(7): p. e70691.

41. Huang, J.-M., et al., Atractylenolide-I sensitizes human ovarian cancer cells to paclitaxel by blocking activation of TLR4/MyD88-dependent pathway. Scientific reports, 2014. 4: p. 3840. 42. Takeda, K. and S. Akira, Toll-like receptors in innate immunity. International immunology, 2005. 17(1): p. 1-14.

43. Perros, F., B.N. Lambrecht, and H. Hammad, TLR4 signalling in pulmonary stromal cells is critical for inflammation and immunity in the airways. Respiratory research, 2011. 12(1): p. 1-8.

44. Noulin, N., et al., Both hemopoietic and resident cells are required for MyD88-dependent pulmonary inflammatory response to inhaled endotoxin. The Journal of Immunology, 2005. 175(10): p. 6861-6869.

45. Brubaker, S.W., et al., Innate immune pattern recognition: a cell biological perspective. Annual review of immunology, 2015. 33: p. 257-290.

46. Takeda, K. and S. Akira, Microbial recognition by Toll-like receptors. Journal of dermatological science, 2004. 34(2): p. 73-82.

47. Tobias, P. and L.K. Curtiss, Thematic review series: the immune system and atherogenesis. Paying the price for pathogen protection: toll receptors in atherogenesis. Journal of lipid research, 2005. 46(3): p. 404-411.

48. Andreakos, E., et al., The toll-like receptor-nuclear factor kappaB pathway in rheumatoid arthritis. Front Biosci, 2005. 10: p. 2478-2488.

49. Schmidt, M., et al., Crucial role for human Toll-like receptor 4 in the development of contact allergy to nickel. Nature immunology, 2010. 11(9): p. 814-819.

50. Wu, F.-x., et al., Intrathecal siRNA against Toll-like receptor 4 reduces nociception in a rat model of neuropathic pain. International journal of medical sciences, 2010. 7(5): p. 251.

51. Tsung, A., et al., Hepatic ischemia/reperfusion injury involves functional TLR4 signaling in nonparenchymal cells. The Journal of Immunology, 2005. 175(11): p. 7661-7668.

52. Powers, K.A., et al., Oxidative stress generated by hemorrhagic shock recruits Toll-like receptor 4 to the plasma membrane in macrophages. The Journal of experimental medicine, 2006. 203(8): p. 1951-1961.

53. Alfonso-Loeches, S., et al., Pivotal role of TLR4 receptors in alcohol-induced neuroinflammation and brain damage. Journal of Neuroscience, 2010. 30(24): p. 8285-8295.

54. Kolek, M.J., et al., Toll–like receptor 4 gene Asp299Gly polymorphism is associated with reductions in

vascular inflammation, angiographic coronary artery disease, and clinical diabetes. American heart journal, 2004. 148(6): p. 1034-1040.

55. Garcia–Rodriguez, S., et al., Increased gene expression of Toll-like receptor 4 on peripheral blood mononuclear cells in patients with psoriasis. Journal of the European Academy of Dermatology and Venereology, 2013. 27(2): p. 242-250.

56. Shaw, P.J., et al., Signaling via the RIP2 adaptor protein in central nervous system-infiltrating dendritic cells promotes inflammation and autoimmunity. Immunity, 2011. 34(1): p. 75-84.

57. Devaraj, S., et al., Demonstration of increased toll-like receptor 2 and toll-like receptor 4 expression in monocytes of type 1 diabetes mellitus patients with microvascular complications. Metabolism, 2011. 60(2): p. 256-259.

58. Roozbehkia, M., et al., The potent suppressive effect of β-d-mannuronic acid (M2000) on molecular expression of the TLR/NF-kB signaling pathway in ankylosing spondylitis patients. International immunopharmacology, 2017. 52: p. 191-196.

59. Kuang, X., et al., Effects of intrathecal epigallocatechin gallate, an inhibitor of Toll-like receptor 4, on chronic neuropathic pain in rats. European journal of pharmacology, 2012. 676(1-3): p. 51-56.

60. Kanuri, G., et al., Cinnamon extract protects against acute alcohol-induced liver steatosis in mice. The Journal of nutrition, 2009. 139(3): p. 482-487.

61. Apetoh, L., et al., Toll-like receptor 4–dependent contribution of the immune system to anticancer chemotherapy and radiotherapy. Nature medicine, 2007. 13(9): p. 1050-1059.

62. Wang, L. and J. Chen, Progress in studies on TLR4 signaling pathway and major depressive disorder. Zhong nan da xue xue bao. Yi xue ban= Journal of Central South University. Medical Sciences, 2017. 42(6): p. 725-729.

63. Abdollahi-Roodsaz, S., et al., Inhibition of Toll-like receptor 4 breaks the inflammatory loop in autoimmune destructive arthritis. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 2007. 56(9): p. 2957-2967.

64. Fekonja, O., M. Avbelj, and R. Jerala, Suppression of TLR signaling by targeting TIR domain-containing proteins. Current Protein and Peptide Science, 2012. 13(8): p. 776-788.

65. Yamamoto, M. and S. Akira, Lipid A receptor TLR4-mediated signaling pathways, in Lipid A in Cancer Therapy. 2009, Springer. p. 59-68.

66. Takeuchi, O. and S. Akira, Pattern recognition receptors and inflammation. Cell, 2010. 140(6): p. 805-820.

67. Yamamoto, M. and K. Takeda, Current views of toll-like receptor signaling pathways. Gastroenterology research and practice, 2010. 2010.

68. Liew, F.Y., et al., Negative regulation of toll-like receptor-mediated immune responses. Nature Reviews Immunology, 2005. 5(6): p. 446-458.

69. Kawai, T. and S. Akira, The role of pattern-recognition receptors in innate immunity: update on Toll- like receptors. Nature immunology, 2010. 11(5): p. 373.

70. Sharifi, L., et al., The Inhibitory Role of M2000 (β-D-Mannuronic Acid) on Expression of Toll-like Receptor 2 and 4 in HT29 Cell Line. Recent patents on inflammation & allergy drug discovery, 2019. 13(1): p. 57-65.

71. Földes, G., et al., Fluvastatin reduces increased blood monocyte Toll-like receptor 4 expression in whole

blood from patients with chronic heart failure. International journal of cardiology, 2008. 124(1): p. 80- 85.

72. Fang, D., et al., Atorvastatin suppresses Toll-like receptor 4 expression and NF-kappaB activation in rabbit atherosclerotic plaques. Eur Rev Med Pharmacol Sci, 2014. 18(2): p. 242-246. 73. Methe, H., et al., Statins decrease Toll-like receptor 4 expression and downstream signaling in human CD14+ monocytes. Arteriosclerosis, thrombosis, and vascular biology, 2005. 25(7): p. 1439-1445.

74. Zhang, G. and S. Ghosh, Negative regulation of toll-like receptor-mediated signaling by Tollip. Journal of Biological Chemistry, 2002. 277(9): p. 7059-7065.

75. Didierlaurent, A., et al., Tollip regulates proinflammatory responses to interleukin-1 and lipopolysaccharide. Molecular and cellular biology, 2006. 26(3): p. 735-742.

76. Loiarro, M., et al., Pivotal Advance: Inhibition of MyD88 dimerization and recruitment of IRAK1 and IRAK4 by a novel peptidomimetic compound. Journal of leukocyte biology, 2007. 82(4): p. 801-810.

77. Narayanan, K.B. and H.H. Park, Toll/interleukin-1 receptor (TIR) domain-mediated cellular signaling pathways. Apoptosis, 2015. 20(2): p. 196-209.

78. Taganov, K.D., et al., NF-κB-dependent induction of microRNA miR-146, an inhibitor targeted to signaling proteins of innate immune responses. Proceedings of the National Academy of Sciences, 2006. 103(33): p. 12481-12486.

79. Boldin, M.P., et al., miR-146a is a significant brake on autoimmunity, myeloproliferation, and cancer in mice. The Journal of experimental medicine, 2011. 208(6): p. 1189-1201.

80. Babazada, H., F. Yamashita, and M. Hashida, Suppression of experimental arthritis with self-assembling glycol-split heparin nanoparticles via inhibition of TLR4–NF-κB signaling. Journal of controlled release, 2014. 194: p. 295-300.

81. Slivka, P.F., et al., A peptide antagonist of the TLR4–MD2 interaction. Chembiochem, 2009. 10(4): p. 645-649.

82. Spiller, S., et al., TLR4-induced IFN-γ production increases TLR2 sensitivity and drives Gram-negative sepsis in mice. The Journal of experimental medicine, 2008. 205(8): p. 1747-1754. 83. Monnet, E., et al., AB0451 NI-0101, a monoclonal antibody targeting toll like receptor 4 (TLR4) being developed for rheumatoid arthritis (RA) treatment with a potential for personalized medicine. 2015, BMJ Publishing Group Ltd.

84. Kashefi, S., et al., A randomized, controlled, phase II clinical trial of β-D-mannuronic acid (M2000) in pre-surgical breast cancer patients at early stage (T1-T2). Clinical and Experimental Pharmacology and Physiology, 2019. 46(6): p. 527-532.

85. Mirshafiey, A., et al., Treatment of experimental arthritis with M2000, a novel designed non-steroidal anti-inflammatory drug. Scandinavian journal of immunology, 2005. 61(5): p. 435-441.

86. Mirshafiey, A., et al., Production of M2000 (β-d-mannuronic acid) and its therapeutic effect on experimental nephritis. Environmental toxicology and pharmacology, 2007. 24(1): p. 60-66.

87. Mortazavi-Jahromi, S.S., et al., Immunopharmacological effect of β-d-mannuronic acid (M2000), as a new immunosuppressive drug, on gene expression of miR-155 and its target molecules (SOCS1, SHIP1) in a clinical trial on rheumatoid arthritis patients. Drug Development Research, 2020. 81(3): p. 295- 304.

88. Gaafar, N.A., A. Razavi, and A. Mirshafiey, β-D-Mannuronic Acid (M2000) as a landmark in Pharmacology. Current drug discovery technologies, 2019.

89. Klaver, E., et al., Trichuris suis soluble products induce Rab7b expression and limit TLR4 responses in

human dendritic cells. Genes & Immunity, 2015. 16(6): p. 378-387.

90. Aletaha, S., et al., M2000 (β-d-mannuronic acid) as a novel antagonist for blocking the TLR 2 and TLR 4 downstream signalling pathway. Scandinavian journal of immunology, 2017. 85(2): p. 122-129.

91. Bakhtiari, T., et al., An in vitro assessment for evaluating the efficiency of β-d-mannuronic acid (M2000) in myelodysplastic syndrome. Journal of cellular physiology, 2019. 234(8): p. 12971-12977.

92. Mirshafiey, A., et al., Introduction of β-d-mannuronic acid (M2000) as a novel NSAID with immunosuppressive property based on COX-1/COX-2 activity and gene expression. Pharmacological reports, 2017. 69(5): p. 1067-1072.

93. Taeb, M., et al., Effect of β-d-mannuronic acid (M2000) on oxidative stress enzymes' gene using healthy donor peripheral blood mononuclear cells for evaluating the anti-aging property. Current drug discovery technologies, 2019. 16(3): p. 265-271.

94. Sharifi, L., et al., Antagonistic Property of G2013 (α-L-Guluronic Acid) on Gene Expression of MyD88, Tollip, and NF-KB in HEK293 TLR2 and HEK293 TLR4. Endocrine, Metabolic & Immune Disorders- Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders), 2019. 19(2): p. 144-149.

95. Mortazavi-Jahromi, S.S., et al., Pharmacological effects of β-d-mannuronic acid (M2000) on miR-146a, IRAK1, TRAF6 and NF-κB gene expression, as target molecules in inflammatory reactions. Pharmacological reports, 2017. 69(3): p. 479-484.

96. Mirshafiey, A., et al., M2000: a revolution in pharmacology. Medical science monitor, 2005. 11(8): p. PI53-PI63.

97. Mirshafiey, A., et al., Novel immunosuppressive therapy by M2000 in experimental multiple sclerosis. Immunopharmacology and immunotoxicology, 2005. 27(2): p. 255-265.

98. Fattahi, M.J., et al., Preclinical assessment of β-d-mannuronic acid (M2000) as a non-steroidal anti-inflammatory drug. Immunopharmacology and immunotoxicology, 2015. 37(6): p. 535-540.

99. Fattahi, M.J., et al., Oral administration effects of β-d-mannuronic acid (M2000) on Th17 and regulatory T cells in patients with ankylosing spondylitis. Biomedicine & Pharmacotherapy, 2018. 100: p. 495-500.

100. Farhang, H., et al., The Immunomodulatory Role of G2013 (α-L-Guluronic Acid) on the Expression of TLR2 and TLR4 in HT29 cell line. Current drug discovery technologies, 2019. 16(1): p. 91-95.

101. Hosseini, S., et al., Anti-aging effects of M2000 (β-D-mannuronic acid) as a novel immunosuppressive drug on the enzymatic and non-enzymatic oxidative stress parameters in an experimental model. Journal of basic and clinical physiology and pharmacology, 2017. 28(3): p. 249-255.

102. Sharifi, L., et al., The role of toll-like receptors in B-cell development and immunopathogenesis of common variable immunodeficiency. Expert review of clinical immunology, 2016. 12(2): p. 195-207.

103. Mirshafiey, A., et al., Anti-aging property of G2013 molecule as a novel immunosuppressive agent on enzymatic and non-enzymatic oxidative stress determinants in rat model. Current drug discovery technologies, 2016. 13(1): p. 25-33.

104. Mortazavi-Jahromi, S.S., et al., Anti-diabetic effect of β-D-mannuronic acid (M2000) as a novel NSAID with immunosuppressive property on insulin production, blood glucose, and inflammatory markers in the experimental diabetes model. Archives of physiology and biochemistry, 2019. 125(5): p. 435-440.

105. Esmaeili-Bandboni, A., M.H. Javanbakht, and A. Mirshafiey, Use of miR-34a, miR-126, and miR-125a- 5p expression level as diagnostic factor and therapeutic target for α-L-guluronic acid and β-D- mannuronic

acid in Type-I diabetic rat models. 2020.

106. Qin, B., et al., MicroRNAs expression in ox-LDL treated HUVECs: MiR-365 modulates apoptosis and Bcl-2 expression. Biochemical and biophysical research communications, 2011. 410(1): p. 127-133.

107. Liu, H., et al., MiR-34a and miR-34c are involved in the pathogenesis of type-2 diabetes by modulating the cell cycle of pancreatic beta-cell. INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL PATHOLOGY, 2016. 9(5): p. 5340-5345.

108. Hosseini, F., et al., Targeting of crosstalk between tumor and tumor microenvironment by β-D mannuronic acid (M2000) in murine breast cancer model. Cancer medicine, 2017. 6(3): p. 640-650.

109. Kashefi, S., et al., The Anti-tumoral Effect of β-D-Mannuronic Acid (M2000) as a Novel NSAID on Treg Cells Frequency and MMP-2, MMP-9, CCL22 and TGFβ1 Gene Expression in Pre-surgical Breast Cancer Patients. Iranian Journal of Allergy, Asthma and Immunology, 2019. 18(1): p. 80-90.

110. Ahmadi, H., et al., The potent inhibitory effect of β-D-mannuronic acid (M2000) as a novel NSAID with immunosuppressive property on anti-cyclic citrullinated peptide antibodies, rheumatoid factor and anti-dsDNA antibodies in patients with rheumatoid arthritis. Current drug discovery technologies, 2017. 14(3): p. 206-214.

111. Fattahi, M.J., et al., Evaluation of the efficacy and safety of β-d-mannuronic acid in patients with ankylosing spondylitis: a 12-week randomized, placebo-controlled, phase I/II clinical trial. International Immunopharmacology, 2018. 54: p. 112-117.

112. Najafi, S., et al., The Effects of Mannuronic Acid on IL-1β, IL-17A, STAT1, and STAT3 Gene Expressions and TLR2 and TLR4 Molecules in Multiple Sclerosis. The Journal of Clinical Pharmacology, 2022. 62(6): p. 762-769.

113. Cho, S.-G., et al., Glutathione S-transferase mu modulates the stress-activated signals by suppressing apoptosis signal-regulating kinase 1. Journal of Biological Chemistry, 2001. 276(16): p. 12749-12755.

114. Nazeri, S., et al., Preclinical and pharmacotoxicology evaluation of α-l-guluronic acid (G2013) as a non-steroidal anti-inflammatory drug with immunomodulatory property. Immunopharmacology and Immunotoxicology, 2017. 39(2): p. 59-65.

115. Mortazavi Jahromi, S.S., et al., Inhibitory effect of G2013 molecule as a novel immunomodulatory agent, on miR-155 gene expression in HEK-Blue hTLR4 cell line. European Journal of Inflammation, 2016. 14(2): p. 86-92.

116. Taeb, M., et al., An in vitro evaluation of anti-aging effect of guluronic acid (G2013) based on enzymatic oxidative stress gene expression using healthy individuals PBMCs. Biomedicine & Pharmacotherapy, 2017. 90: p. 262-267.

117. Fard, N.A., et al., Efficacy and safety of G2013 as a novel immunosuppressive agent on differentiation, maturation and function of human dendritic cells. Iranian Journal of Public Health, 2017. 46(2): p. 216.

118. Sharifi, L., et al., Immunomodulatory effect of G2013 (α-L-Guluronic acid) on the TLR2 and TLR4 in human mononuclear cells. Current Drug Discovery Technologies, 2018. 15(2): p. 123-131.

119. Hajivalili, M., et al., G2013 modulates TLR4 signaling pathway in IRAK-1 and TARF-6 dependent and miR-146a independent manner. Cellular and molecular biology, 2016. 62(4): p. 1-5.

120. Mirshafiey, A., et al., Evaluation of the effect of α-L-guluronic acid (G2013) on COX-1, COX-2 activity and gene expression for introducing this drug as a novel NSAID with immunomodulatory property. Recent patents on inflammation & allergy drug discovery, 2018. 12(2): p. 162-168.

121. Abolhassani, H., et al., Autoimmune phenotype in patients with common variable immunodeficiency. J Investig Allergol Clin Immunol, 2013. 23(5): p. 323-9.

122. Sharifi, L., et al., Immunomodulation of TLR2 and TLR4 by G2013 (alfa-L-Guluronic acid) in CVID Patients. International Journal of Pediatrics, 2017. 5(7): p. 5327-5337.

123. Afraei, S., et al., New therapeutic approach by G2013 in experimental model of multiple sclerosis. Acta Neurologica Belgica, 2015. 115(3): p. 259-266.

124. Hosseini, F., et al., Anti-inflammatory and anti-tumor effects of α-l-guluronic acid (G2013) on cancer-related inflammation in a murine breast cancer model. Biomedicine & Pharmacotherapy, 2018. 98: p. 793-800.

125. Noorbakhsh, S.M., et al., Effects of guluronic acid (G2013) on gene expression of TLR2, TLR4, MyD88, TNF-α and CD52 in multiple sclerosis under in vitro conditions. Immunopharmacology and Immunotoxicology, 2019. 41(6): p. 586-590.

126. Khadem Azarian, S., et al., A randomized clinical trial for the assessment of the efficacy and safety of guluronic acid (G2013) in patients with rheumatoid arthritis. Immunopharmacology and immunotoxicology, 2019. 41(1): p. 95-101.

127. Khadem Azarian, S., et al., Effects of guluronic acid, as a new NSAID with immunomodulatory properties on IL-17, RORγt, IL-4 and GATA-3 gene expression in rheumatoid arthritis patients. Immunopharmacology and Immunotoxicology, 2020. 42(1): p. 22-27.

128. Bakhtiari, T., et al., Effect of Guluronic Acid (G2013), As a New Anti-inflammatory Drug on Gene Expression of Pro-inflammatory and Anti-inflammatory Cytokines and Their Transcription Factors in Rheumatoid Arthritis Patients. Iranian Journal of Allergy, Asthma and Immunology, 2019: p. 1-10.

129. Mortazavi-Jahromi, S.S., et al., Assessment of immunological profile in ankylosing spondylitis patients following a clinical trial with guluronic acid (G2013), as a new NSAID with immunomodulatory properties. Immunologic research, 2019. 67(1): p. 108-115.

130. Nazeri, S., et al., The safety and efficacy of Guluronic acid (G2013) in ankylosing spondylitis: A randomized controlled parallel clinical trial. Pharmacological Reports, 2019. 71(3): p. 393-398.

131. Tavasolian P, Sharifi L, Aghamohammadi A, Noorbakhsh F, Sanaei R, Shabani M, et al. Toll-like receptors pathway in common variable immune deficiency (CVID) and X-linked agammaglobulinemia (XLA). Eur Cytokine Netw. 2018;29(4):153-8.

132. Sharifi L, Aghamohammadi A, Rezaei N, Yazdani R, Rezaei F, Bokaie S, et al. Interleukin-1β and interleukin-6 in Common Variable Immunodeficiency and their association with subtypes of B cells and response to the Pneumovax-23 vaccine. Eur Cytokine Netw. 2019;30(4):123-9.

133. Saadat P, Noorbakhsh M, Beladi Moghadam N, Babarykin D, Smirnova G, Najafi S, et al. Efficacy and Safety of Guluronic Acid (G2013) in a Randomized, Controlled Phase II Clinical Trial on Patients with Multiple Sclerosis. Biomed J Sci & Tech Res, BJSTR. 2022.47.007552.

134. Rezaieyazdi Z, Farooqi A, Soleymani-Salehabadi H, Ahmadzadeh A, Aslani M, Omidian S, et al. International multicenter randomized, placebo-controlled phase III clinical trial of β- *D-mannuronic acid in rheumatoid arthritis patients. Inflammopharmacology. 2019;27(5):911-21.*

Applied Sciences Research Periodicals
May 2023, Vol. 1, No. 2, pp. 31-37

Feasibility Study of Solar PV System for Backup Application: A Case in Dilla University Water Pump System

Eneyw Gardie Damtiea, and Habtamu Dubale

1. School of Mechanical and Automotive Engineering, College of Engineering and Technology, Dilla University, P.O. Box 419, Dilla, Ethiopia

Abstract:
Solar energy generation utilizes solar cells or photovoltaic cell devices to convert the energy of light directly into electricity. In recent, it has been proved that the population increased and the need for energy and its related services to satisfy human social and economic development and health is increasing. At this time, most institutions and business firms use backup generators for backup applications. This study focuses on renewable energy production as well as the storage system for running water pumps found in Dilla University, Odaya Campus. The use of this fuel generator has various economic, social, and environmental impacts. This includes the higher cost of fuel, air pollution for global warming, and maintenance costs. This research intends to design a Solar PV and study the feasibility of the system for backup applications. Finally, this potential contributes to fill the energy gap between the demand and supply of the country mainly at Dilla University. In designing and studying this hybrid system we have gained a payback period of four years. This implies that once investing the required initial capital, we can use the system for over fifteen years with only maintenance costs.

Keywords: Photovoltaic, Solar Energy, Radiation, Module

INTRODUCTION

Solar energy generation utilizes solar cells or photovoltaic cell devices to convert the energy of light directly into electricity. In recent, it has been proved that the population increased and the need for energy and its related services to satisfy human social and economic development and health is increasing. Most developing countries are poor in conventional fossil fuel resources and have to import them. One of the most versatile, renewable, and environment-free energy sources is the solar PV system. Since it has no moving parts in the system, it will have a low maintenance cost as compared to a fuel generator [1, 2]. So, a decentralized system of solar equipment installed at the village level is one of the technically feasible solutions. Solar power offers many advantages in the generation of electricity. Even though it has a high initial investment cost, it will pay back in a short time and it will be a feasible energy choice for the backup application [3, 4].

In Ethiopia, most of the critical infrastructure that communities depend on in universities, hospitals, and community shelters relies almost exclusively on diesel generators when the grid goes down. Unfortunately, diesel generators aren't always up to the task when called upon. Among these institutions, Dilla University is a former institution in Ethiopia that uses a diesel generator backup for grid downtime. This paper assesses a feasibility study for solar energy usage in Dilla University instead of a backup generator. This is achieved by taking the water pump generator which is on standby 24/7 and designing the solar power needed. The study aimed at finding and verifying a way that shows how the university can use solar energy sources efficiently to produce electricity, reducing its dependence on oil according to the collected data.

RELEVANT LITERATURE REVIEW

Photovoltaic (PV) technology is used for generating electricity from incoming solar radiation. Several attempts have been made to evaluate, monitor, and improve the performance of different components of a PV system [5].

The most efficient use of solar energy is when the panels are directly connected to the load. The success of water pumping lies partly in the elimination of the intermediate phase, namely the battery bank, for energy storage. With a direct connection between the PV array and the pump, water can be pumped during sunlight hours. The most efficient form of direct-connect systems is when the water is being pumped to an elevated storage tank, thus the electrical energy from the panels is converted to the potential energy of the elevated water, to be used on-demand, often by gravity. The overall efficiency, from sunlight to water flow, has been recorded to exceed 3% [6, 7].

The system is an easy-to-implement and environment-friendly solution for irrigating fields. The system was found to be successful when implemented for boreholes as they pump over the whole day. Solar pumps also offer clean solutions with no danger of borehole contamination. The system requires minimal maintenance and attention as they are self-starting. To further enhance the daily pumping rates tracking arrays can be implemented. The main advantage of this project is optimizing power usage through water resource management and also saving the government's free subsidiary electricity. This proves an efficient and economical way of irrigation and this will automate the agriculture sector [8, 9].

On the other hand, the solar PV system is used in thermal pumping systems. Delgado-Torres (2007) reviewed the thermal energy of a water pumping system and the different types of solar thermal energy based on thermodynamic methods. While a simple solar thermal water pumping system usually has low effectiveness and low output power, there are two alternatives for thermo-mechanical conversion; conventional that the pump is moved by mechanical energy, and unconventional in which the specially designed system of water pumping is driven by mechanical energy [10].

Harishankar et al., (2014), this study demonstrates the feasibility study and demonstration of using a solar PV system to provide energy for the pumping requirements for Dilla University water consumption. Even though there is a high capital investment required for this system to be implemented, the overall benefits are high and in long run, this system is economical [11]. Mohammed M (2001), After economic analysis, it is shown that the Photovoltaic pumping system for the water pump is more feasible than a Diesel engine pumping system. From an economic viewpoint, the PV pumping system for only one season of irrigation is a little bit higher than the diesel engine pumping system due to the high cost of the PV modules and their components [12]. The automation of an irrigation system will largely reduce the gap between requirement and consumed energy and further conserve resources thereby reducing the wastage of resources.

MATERIALS AND METHODS

The method is a procedure or set of rules and principles of intellectual operations to analyze to achieve the result using scientific analysis. It is a set of principles leading all organized projects and research, allowing selection and coordination of the project. In this study, the methods implemented are listed in figure 1.

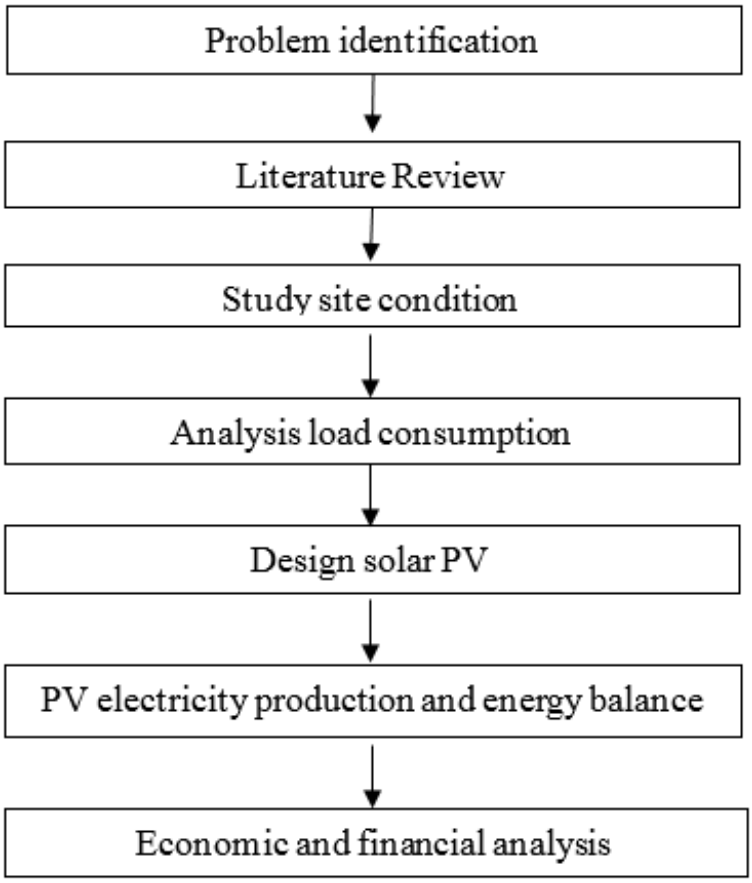


Fig. 1 Project Methodology

PV system design is the process of determining the size of each component of a standalone photovoltaic power system to meet the load requirement.

The designing is done through the following steps;
Step 1: Site inspection
Step 2: Determining load requirements
Step 3: PV module sizing
Step 4: Charge controller sizing
Step 5: Battery bank sizing
Step 6: Inverter Sizing
Step 7: Cable size

Site inspection is the most important in the design because it helps to determine whether a stand-alone system is viable or not. The factors influencing power generation from the PV system are irradiation and temperature. At constant temperature power generation from PV System increases with increasing irradiation so the site location should be inspected to know the number of sun day per year as shown in table 1.

Table 1. Geographical details.

Descriptions	Details	Units
Location	Dilla	
Longitude	6°24'30"N	
Latitude	38°18'30"E	
Elevation	1570	Meters
Solar radiation	5.55	kWh/m^2/day
Area	583.2	m^2
Ground mounting	Fixed	

The major components of solar PV systems are solar charge controllers, inverters, battery banks, auxiliary energy sources, and loads (appliances) [13]. Figure 2 shows the solar PV system components that are designed for the backup application in the case of the Dilla university water pump.

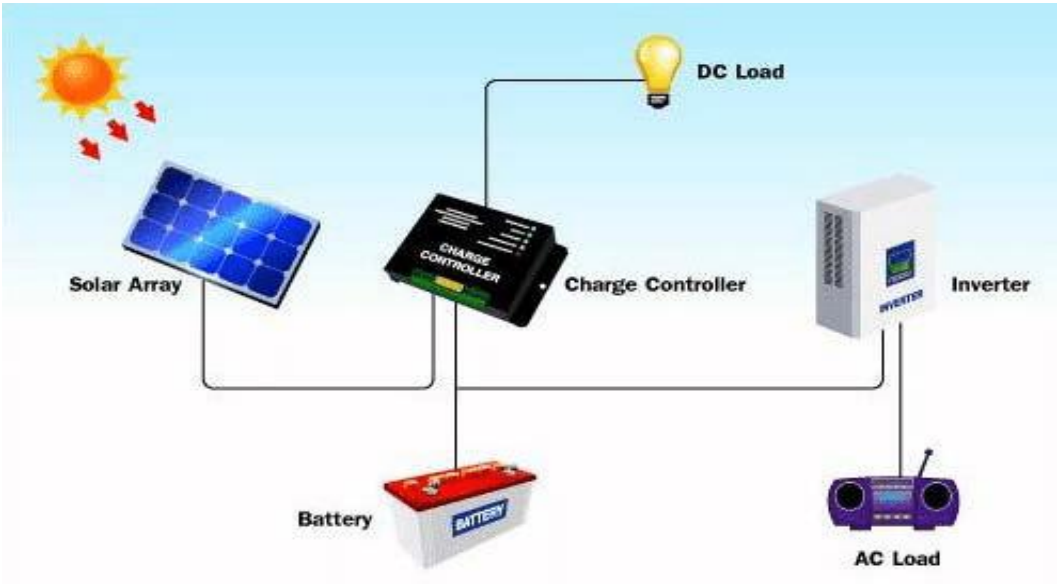


Fig. 2 Solar-powered water pump components

The first step in designing a solar system PV system is to find out the total power and energy consumption of all loads that need to be supplied by the solar PV system.

Total power use per day=Total appliances uses power in watt per day (1).

Total energy consumption per day=Total appliances use in watt-hours per day (2).

Now the total PV panels energy required=Total energy consumption per day x 1.3 (3) Where 1.3 is the loss factor of the system [14, 15].

In estimating the total watt-peak rating needed for the PV modules to operate the pump motor, the total watt-hours per day needed from the PV module is divided by the Panel Generating Factor (PGF) [15, 16].

Panel generating factor (PGF) = solar radiation × total correction factor on the solar panel

An inverter is needed in the solar home system to change the DC input signal from the battery to its appropriate AC signal for the power outlets. The input rating of the inverter should never be lower than the total watt of the appliances.

The inverter must have the same nominal voltage as your battery [13, 17, 18]. The input rating of the inverter should be 25-30% bigger than the watt of the pump.

$$\text{Inverter size} = \text{total watt} \times \frac{130\%}{100\%}$$

Solar battery sizing is one of the most important considerations when choosing the basic components of your stand-alone solar electric system.

The main objective when sizing a battery bank is to get one energy that can handle the load coming from your PV panel array and provide enough stored power for your needs when there is no sunshine [18, 19]. The battery capacity should be large enough to store sufficient energy to operate the appliances at night and cloud day.

$$\text{Size of battery} = \frac{\text{C} \times \text{n}}{0.85 \times 0.6 \times \text{Vsystem}}$$

All the required components are designed and selected for this study. Table 2 shows the specification and the parameters designed to perform this plant in Dilla university for backup application.

Table 2 Results obtained from sizing the PV system

Component	Description of Component	Result
Load estimation	Total estimated load	384800Wh
PV array	Array capacity	8040 W
	Number of modules in series	2
	Number of modules in parallel	12
	Total number of modules	24
Battery Bank	Battery bank capacity	7859.47Ah
	Number of batteries in series	8
	Number of batteries in parallel	5
	Total number of batteries required	40
Voltage Regulator	The capacity of voltage regulators required	59A
	Number of voltage regulators required	1
Inverter	Capacity of inverter	60KVA
Wire	Between the PV module and batteries through the voltage regulator	59A $1.688mm^2$
	Between the battery bank and inverter	236A, $34mm^2$
	Between inverter and load	78A, $4mm^2$

In designing the solar PV system for the backup application, it requires higher initial capital, but once the system is installed it is higher economical. So let us compare it with the fuel cost of the generator system to make sure if the PV system is relatively higher cost.

The PV system guarantee is 25 years this implies that there will be saving money for 22 years as well as the initial cost of the traditional generator system. From here it is well seen that a decentralized solar power system is one of the solutions for our future demand for energy for backup and standalone applications without environmental degradation and it will be at a lower cost as shown in table 3.

Table 3 Feasibility study.

Details	Qty in liter	Units	Cost in birr
Diesel Consumption			
Diesel consumption per hour	10	Liter	670
Diesel consumption per day	80	Liter	5360
Diesel consumption per month	2400	Liter	160,800
Diesel consumption per year	28800	Liter	1,929,600
Subtotal			13305560
Contingency (%5)	1,929,600×0.05		96,480
Total	1,929,600+96,480		2,026,080
Solar panel System Investment			
Total			6,684,493.2
Payback period /year			4 years

CONCLUSION

The location of the site at Dilla 6°24′30″N, 38°18′30″E was suitable for solar PV from the candidate locations. This is mainly due to it being the nearest, low slope, a short distance from roads, far from town, far from the forest, and far from the stream. This potential contributes to fill the energy gap between the demand and supply of the country. It is also used to bridge the energy gap between rural and urban communities if the country starts to use this high green solar potential to generate power needs. The Majority of areas fulfilled the suitability analysis criteria. Solar irradiance, slope, soil type, land use, land cover, and distance from roads, forests, towns, streams, and schools were the determinant factors for solar PV power site suitability analysis. This study focuses on renewable energy production as well as the storage system for running water pumps found in Dilla University, Odaya Campus. The use of this fuel generator has various economic, social, and environmental impacts. This includes the higher cost of fuel, air pollution for global warming, and maintenance costs. From this study it is clear that to conclude that, this potential contributes to fill the energy gap between the demand and supply of the country mainly at Dilla University. In designing and studying this hybrid system we have gained a payback period of four years. This implies that once we invest the required initial capital, we can use the system for over fifteen years with only maintenance costs.

REFERENCE

1. Muluken Zegeye, Tassew Tadiwos, Abdulkadir Aman, Optimal sizing of solar water pumping system for small scale irrigation: A case study of Dangila. International Journal of Renewable and Sustainable Energy, 3(5): 99-107, (2014).

2. A. Castillo and D. F. Gayme, "Grid-scale energy storage applications in renewable energy integration: A survey," Energy Conversion and Management, vol. 87, pp. 885-894, 2014.

3. Kumarasamy, S., Tulika, S., Guddy, S. and Manicam, P. Modeling and Estimation of Photosynthetic ally Active Incident Radiation Based on Global Irradiance in Indian Latitudes. IJEEE. 4, 21 (2013).

4. Idowu, O.S., Olarenwaju, O.M. & Ifedayo, O.I. Determination of optimum tilt angles for solar collectors in a low-latitude tropical region. Int J Energy Environ Eng 4, 29 (2013).

5. Glasnovic, Z, Margeta, J., A model for optimal sizing of photovoltaic irrigation water pumping systems. Solar Energy, 81(2007).

6. Turlough Guerin, A case study identifying and mitigating the environmental and community impacts from construction of a utility-scale solar photovoltaic power plant in eastern Australia. Solar Energy, Volume 146, April 2017, Pages 94-104.

7. Grid-connected PV systems design guidelines for accredited designers, clean energy council l (CEC), Issue 3 July 2007, updated November 2009.

8. Esan Ayodele Benjamin, Egbune Dickson, Estimating the solar home system sizing for rural residential apartments using a panel tilt angle of 82 degrees. Ilorin, Kwara State as Case Study American Journal of Electrical and Computer Engineering Volume 1, Issue 2, December 2017, Pages: 90-96.

9. Wudil, Kano State, M. Ishaq, U. H Ibrahim, H abubakar, Design of an off-grid photovoltaic system: a case study of government technical college. International journal of scientific and technology research volume 2, Issue 12, 2013.

10. Delgado-Torres AM. Solar thermal heat engines for water pumping: an update. Renewable and Sustainable Energy Reviews 2009;13(2):462–72.

11. Harishankar S., Sathish Kumar R., Sudharsan K.P., Vignesh U., and Viveknath T., Solar Powered Smart Irrigation System. Advance in Electronic and Electric Engineering, Vol. 4(4), pp.341-346, 2014.

12. Mohammed Mozammel Haque, Photovoltaic Water Pumping System for Irrigation. 4th International Conference on Mechanical Engineering, December 26-28, 2001, Dhaka, Bangladesh/pp. I 21-26.

13. Ewnetu Tefera,Velmurugan Paramasivam, Eneyw Gardie , Habtamu Dubale, Senthil Kumaran Selvaraj, Experimental investigation of suitable thin layer drying curve to solar maize dryer assisted for biomass back-up heater, Materials Today: Proceedings Volume 46, Part 17, 2021, Pp 7389-7395.

14. Abdallah S., The effect of using sun-tracking systems on the voltage-current characteristics and power generation of flat-plate photovoltaics. energy conversion and management, Vol. 45, pp. 1671-1979, 2004.

15. M. N. Lakhoua, et al., "System Analysis of a Hybrid Renewable Energy System," International Journal of Electrical and Computer Engineering (IJECE), vol. 4, no. 3, pp. 343-350, 2014.

16. Sravankumar Jogunuri, Ravish Kumar, Deepak Kumar, Sizing an off-Grid Photovoltaic System. International conference on energy, communication, data analytics, and soft computing (ICECDS) 2017.

17. Kumar, Jerry & Ram, Nanik & Panjwani, Manoj & Khan, Danish. (2021). Design and performance analysis of PV grid-tied system with the energy storage system. International Journal of Electrical and Computer Engineering. 11. 1077-1085.

18. M. K. Panjwani, et al., "Hybrid concentrated photovoltaic thermal technology for domestic water heating," Indonesian Journal of Electrical Engineering and Computer Science (IJEECS), vol. 16, no. 3, pp. 1136-1143, 2019.

19. Mohammad Baqir, Harpreet Kaur Channi, Analysis and design of solar PV system using PVsyst software, Materials Today, Volume 48, Part 5, 2022, Pages 1332-1338.

Applied Sciences Research Periodicals
May 2023, Vol. 1, No. 2, pp. 38-65

Petrographic Analysis of Rock Samples in Bui Division North West Region of Cameroon: Implications on Water Mineralization and Classification

Fondzenyuy Vitalis Fonfo[1], and Fondzenyuy Lionel Nyanchi[2]

1. University of Dschang, Faculty of Science, Department of Earth Sciences, P.O Box 67 Dschang
2. University of Bamenda, College of Technology

Abstract:
Percolation of water through rock samples is the main agent of the chemical weathering of most rocks. The rock- water interactions are identified as the main process responsible for water mineralization. The ionic content of any water source is dominantly expected to be as a consequence of these interactions. These assertions were verified in this work. In a bid to determine the possible ions in any water source and obtain its water type, a petrographic analysis of the rock samples within the water source vicinity and the geological set up of the entire zone is imperative. To put into evidence this inference, five water catchments, 29 boreholes. 16 Open wells, 16 rivers and 16 streams were studied in this work. Scrupulously sampling in accordance to the norms of the art was done and water samples taken immediately to the Laboratory for physico-chemical analysis. A petrographic analysis of the rock samples from Bui division was done using Dave's method in which thin section slides were prepared from the rocks for a microscopic identification of the minerals present. The rocks were basalts, trachytes, rhyolites, ignimbrites, phonolites and scoria characteristic of the dominant volcanic area, with granites in some plains. Water samples were analysed to deduce the relationship between the ions present and their origin from the dissolution of the rock minerals. Nonetheless, there is a likelihood of ions to be present in water sources from anthropogenic sources, but the aim of this article is to discern if the ions in water are dominantly from rock mineral dissolution or from other sources. The ions in the water samples were used to determine the main water type in Bui division. From the rock thin sections, the Modal composition of each rock type was also established. At the end of this research, it was emphatically revealed that rock-water interactions and the resultant mineral dissolution was the main mechanism responsible for mineralization of water sources in Bui division.

Keywords: Rock type, minerals, dissolution, petrography, water type

INTRODUCTION

The qualitative and quantitative importance of water sources remains of primordial concern in communities worldwide. An evaluation of water sources to determine their chemical compositions, the water types and their suitability for diverse purposes such as drinking, domestic and agriculture remain preoccupying. Water mineralization is due to the presence of ions derived from anthropogenic and natural sources such as water rock interactions involving dissolution of rock minerals. Application of chemical fertilizers remains one of the main anthropogenic sources of introducing some ions into water sources, but for this to be a dominant source; there must be a large-scale industrial application of fertilizer absent in Bui division. Based on this assertion the main objective of this work was to trace and put into evidence the fact that most water mineralization is as a consequence of dissolution of rock minerals. The ions determined will also be used to determine the water type. Rock samples representative of the entire division were

collected and thin rock sections prepared according to the Dave's method. From these thin sections, microscopic observations were done to identify the minerals present in the rocks. The chemical compositions of the identified minerals were well determined with their relevant chemical formulae. With these known compositions relevant chemical equations were written that chemically expressed the mineral dissolutions to release into the water bodies the different ions. The ions present were revealed via a physicochemical analysis of the studied representative water samples (Dechao et al., 2020; Muhammed et al., 2020; Fondzenyuy and Kengni, 2021). This analysis in most communities has become increasingly important and has same implications in Bui division of the North West Region of Cameroon (WHO, 2017, 2018, 2019). In the same vein many works on water quality evaluation for suitability in diverse purposes through analysis of water mineralization has been done worldwide. Water related studies indicate that human activity and influence on physico-chemical variables can compromise water quality (Sajil et al., 2014; Tyagi et al., 2014; Njoyim et al., 2016 a; Inam et al., 2017; Germain et al., 2019). Population growth, economic activity and urbanization of most settlements, has an impact on the water sources.

The chemistry of most water sources done by (Ramesh and Elango, 2012; Akoachere et al., 2019; Frommen et al., 2019), highlight chemical reactions inherent with; soil- water interactions, dissolution of primary minerals, rock- water interactions and anthropogenic sources to be at the origin of ions in water bodies. This is further expressed in some detailed works on geochemical evolution of water (Edmunds and Smedley, 1996; Tanyileke et al., 1996; Deutsch, 1997; Appelo and Postma, 2005).

The objective of this study was to establish the mineralogy of the Bui rock samples and determine the ions present in the studied water samples. Specifically, thin rock sections revealed the minerals present while the physico- chemical results gave the ions in the water samples. The variables; Temperature (oC), and pH, EC, were obtained insitu, while Na^+, K^+, Ca^{2+}, Mg^{2+}, HCO_3^-, NO_3^-, Cl^-, SO_4^{2-}, SiO_2 were obtained in the Laboratory using the Hanna Instrument HI83200 Multiparameter Photometer. This instrument is innovative, reliable and cost effective in its application as compared with the traditional titrimetric methods with many cumulative minor error margins.

LOCATION OF THE STUDY ZONE

Bui division has boundaries, with Donga Mantung to the North, Ngohketunjia to the South, Boyo to the West, and Noun division to the East. The location of Bui division and the Geology of the study site are presented in Fig.1, while a cross section of the rock outcrop in the study area is illustrated in Fig.2.

GEOLOGY (LITHOLOGY)

The Bamenda highland in which Bui division is part has a granitic basement covered by basalts and trachytes from tertiary volcanicity in the Cameroon Volcanic Line (Ngako et al., 2008). The division is part of the Bamenda highlands, a northward extension of the Bambouto Mountain part of the continental Cameroon Volcanic Line (C.V.L). The dominant geologic formations of Bui are basalts and trachytes similar to those of the Bamenda Mountain as reported by (kamgang, 2003). In these works, the Bambouto Mountain is reported to be of volcanic origin similar to its northern extension the Bamenda highlands in which Bui the study area is found. These results are in agreement with the field observations indicating that trachytes and basalts are the dominant rock

types in Bui. To these rocks are often associated phonolites, rhyolites and ignimbrites. A summary of the minerals in the volcanic rocks of Bui division are presented in Table I.

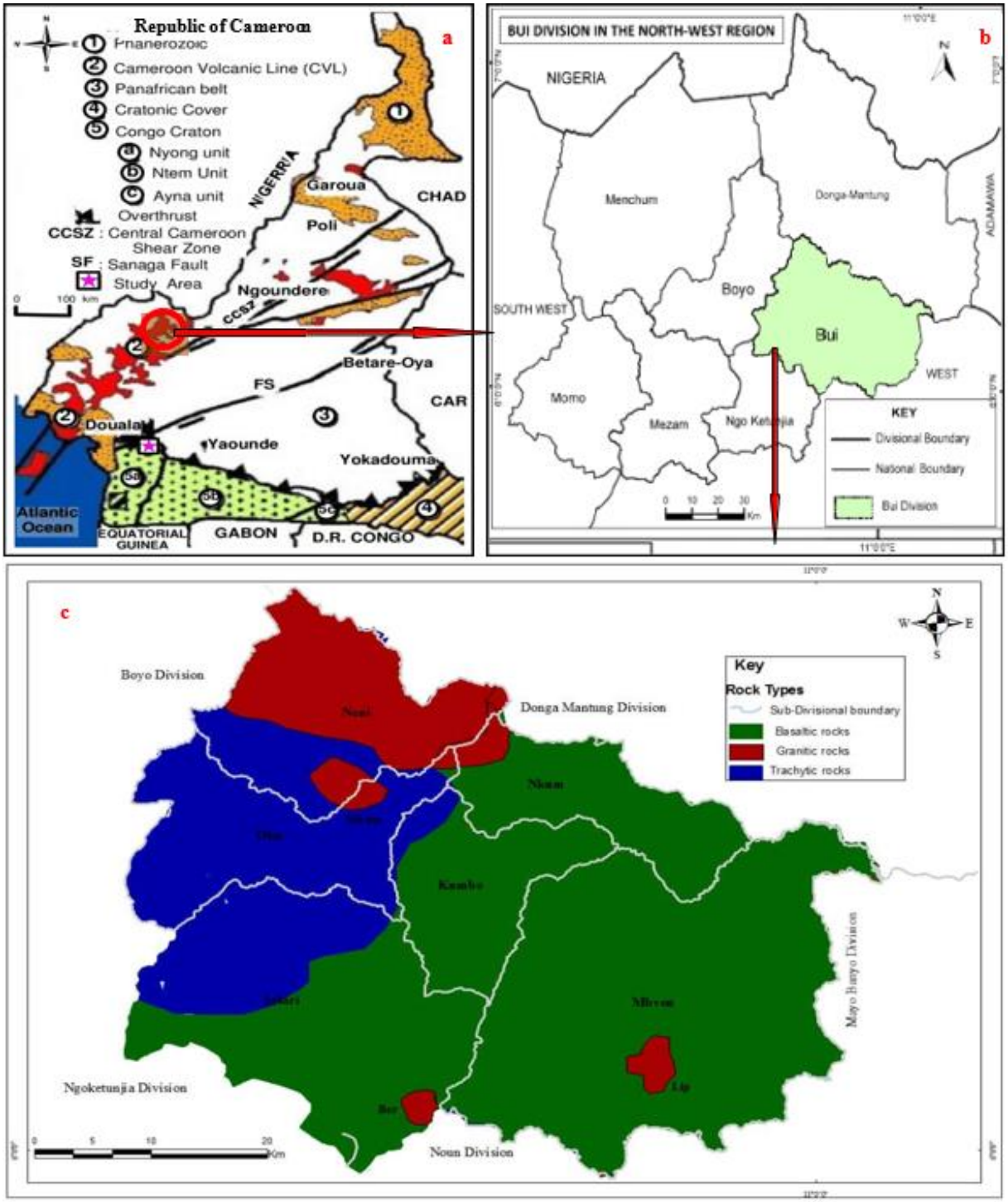


Fig. 1: (a)Site in Cameroon (b) Bui division (c)The geologic map of Bui Division

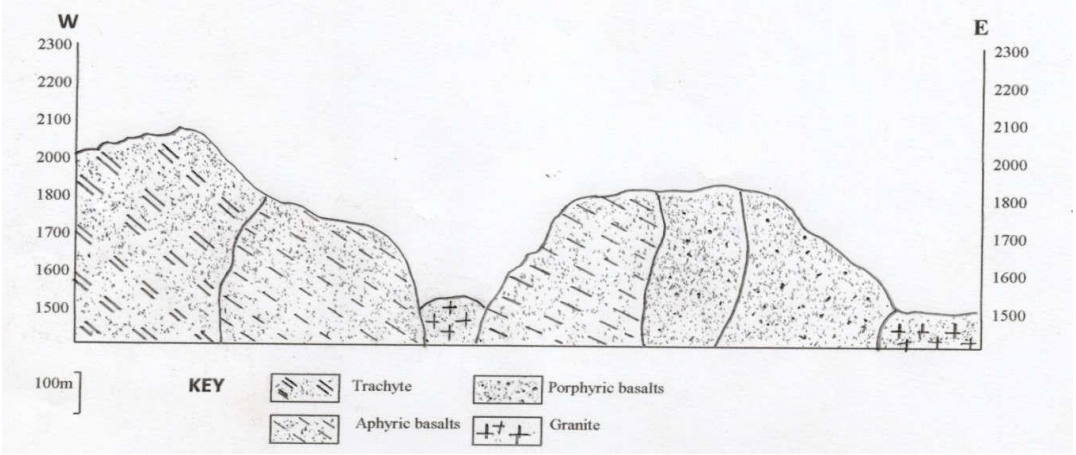


Fig. 2: Cross section of rock outcrop in the study area

Table I: Summary of the minerals in the volcanic rocks of Bui Division

Rock	Minerals
Basalt	Plagioclase Olivine, pyroxene
Trachyte	Plagioclase Alkaline feldspar, pyroxene, amphibole, biotite
Rhyolite	Plagioclase Alkaline feldspar, quartz, amphibole, biotite
Phonolite	Pyroxene
Ignimbrite	Plagioclase Quartz, biotite, alkaline, feldspar, pyroxene, rocky inclusions

The mineralogy of the rock samples of the study sites from the theoretical perception are presented in Table II.

Apart from the basalts and trachytes that are widespread in Bui Division, rhyolites, phonolites, ignimbrites and scoria also accompany these volcanic rocks. The mineralogy of the associated volcanic rocks was presented in Table III.

These mineralogic presentations were based on the understanding of the mineral constituents of the specific rock types and their known chemical compositions (Whitten and Brooks, 1978). These were confirmed in the petrographic studies done in this work.

Table II: Mineralogy of the rock samples from the study sites

SITES	Rock types	Minerals	Chemical composition
ELA	Trachytes	Alkaline feldspars Pyroxene(augite) Amphibole(hornblende) Biotite	$NaAlSi_3O_8$ $KAlSi_3O_8$ $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$ $NaCa_2(Mg, Fe^{2+})_4(Al, Fe^{3+})(SiAl)_8O_{22}(OH, F)_2$ $(K (Mg, Fe), (AlSi_2O_{10}) (OH)_2$
MBI	Basalts	Olivine Calcite Pyroxene (augite) Apatite	Mg_2SiO_4 Fe_2SiO_4 $CaCO_3$ $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$ $Ca_2Cl_5(PO_4)_3$
BEL	Basalts	Olivine	Mg_2SiO_4 Fe_2SiO_4

		Calcite Pyroxene (augite) Apatite	$CaCO_3$ $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$ $Ca_2Cl_5(PO_4)_3$
NKA	Basalts	Olivine Calcite Pyroxene (augite) Apatite	Mg_2SiO_4 Fe_2SiO_4 $CaCO_3$ $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$ $Ca_2Cl_5(PO_4)_3$
YEH	Basalts	Olivine Calcite Pyroxene (augite) Apatite	Mg_2SiO_4 Fe_2SiO_4 $CaCO_3$ $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$ $Ca_2Cl_5(PO_4)_3$

Source: (Whitten and Brooks, 1978).

Table III: Minerlogical composition of associated volcanic rocks

Rock type	Minerals	Chemical composition
Rhyolite	Quartz Pyroxene Alkaline feldspars	SiO_2 $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$ $NaAlSi_3O_8$ –$KalSi_3O_8$
Ignimbrite	Quartz Biotite Pyroxene	SiO_2 $(K (Mg, Fe), (AlSi_2O_{10}) (OH)_2$ $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$
Phonolite	Olivine Calcite Pyroxene (augite) Apatite	Mg_2SiO_4 Fe_2SiO_4 $CaCO_3$ $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$ $Ca_2Cl_5(PO_4)_3$
Scoria	Plagioclase Pyroxene	$NaAlSi_3O_8$ $CaAl_2Si_2O_8$ $(Ca, Mg, Fe, Al)_2(Al, Si)_2O_6$

Source: (Whitten and Brooks, 1978).

The susceptibility of the various minerals in the rocks to weathering are generally in the order; glass > olivine > pyroxene > amphibole > plagioclase > k-feldspar (orthoclase) according to (Richard *et al*., 1987). From the weathering of these minerals the water samples were expectedto have the following ions in solution to be revealed in the laboratory analysis: $Si^{4+,}$ Na^+, K^+, Mg^{2+}, Ca^{2+}, Fe^{2+}, Fe^{3+}, Al^{3+}, Cl^-, HCO_3^-, CO_3^{2-}. Water samples were collected from open wells, boreholes, streams and rivers that have same geologic characteristics to the catchment areas except boreholes in GS Wasi ($BH4_a$), GS Tan ($BH4_b$), GS Kwanso, ($BH4_c$), GS Lip ($BH2_e$) and rivers in Kumbo RW5 within granitic environments with their characteristic minerals indicated below, (Whitten and Brooks, 1978).

Granites; Quartz (SiO_2), feldspars ($NaAlSi_3O_8$. $CaAl_2Si_2O_8$)
Amphiboles and hornblende ($NaCa_2 (Mg, Fe)_4(AlFe) (Si. Al)_8O_{22} (OH, F)_2$
Mica (biotite, $K (MgFe), (AlSi_3) O_{10} (OH, F)_2$ and
Muscovite, $KAl_2 (AlSi_3O_{10}) (OH, F)_2$.

MATERIALS AND METHODS

Materials

Aphyric and Porphyritic Basalts:

Aphryic basalts, dark in colour outcrop in Kumbo and Jakiri subdivisions Fig.3 a, b. In Mbven (MBI) and Nkum (BEL) Subdivisions, porphyritic basalts outcrop and are fairly dark in colour with olivine

phenocryts Figs.3 c and d. The rock sample borders are highly oxidized producing reddish oxides, Fig .3 c and d.

Trachytes:

The trachyte outcrops in Elak and Tolon in Oku Subdivision Fig. 4 were light and greyishin colour with a vitreous lustre and aphyric in texture.

Ignimbrite:

They were made up of vesicles containing fiammes, quartz and other rock fragments as a result of ignimbritic dynamism (an acidic flow that becomes less viscous due to richness in gas). It was a variety of hardened tuff made up of glass shard (glass fragments) ground mass. Bamenda highlands Ignimbrites are greenish to whitish in colour resulting from the welding upof volcanic fragments; Fig .5.

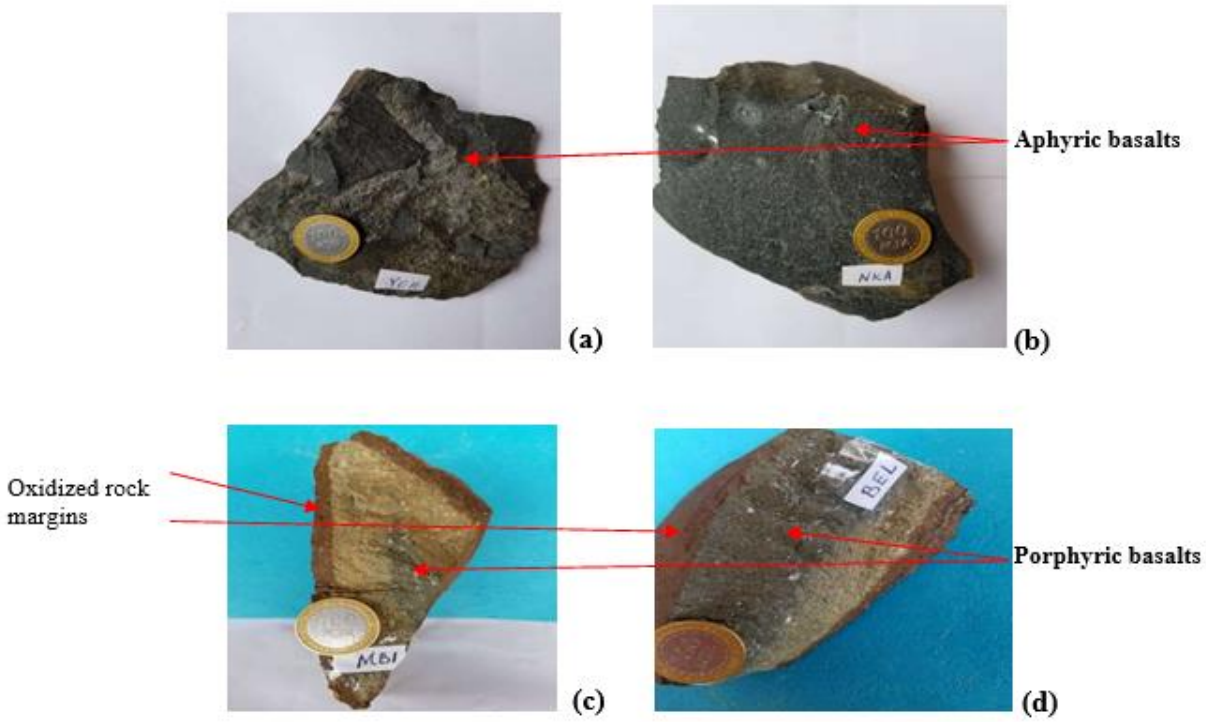


Fig .3: Aphyric basalts (a) Kumbo (b) Jakiri Subdivisions Porphyric basalts (c) Mbven (d) Nkum Subdivisions

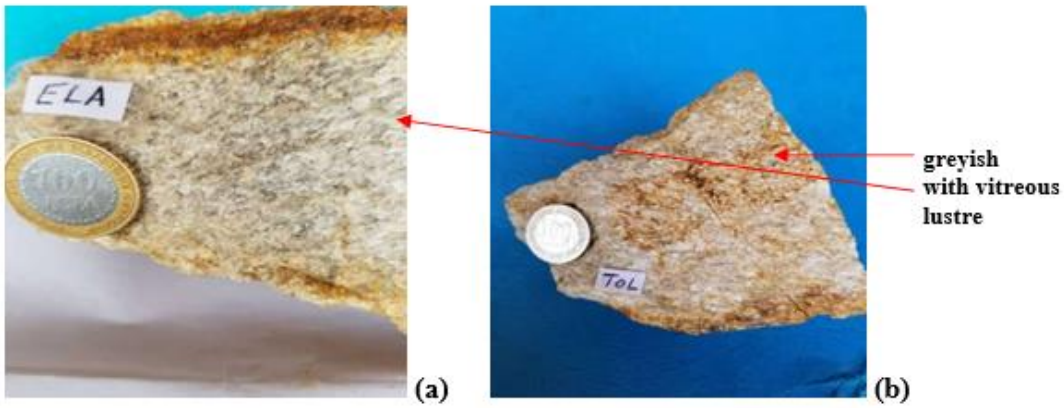


Fig .4: Trachytes from Oku Subdivision (a) Elak (b) Tolon

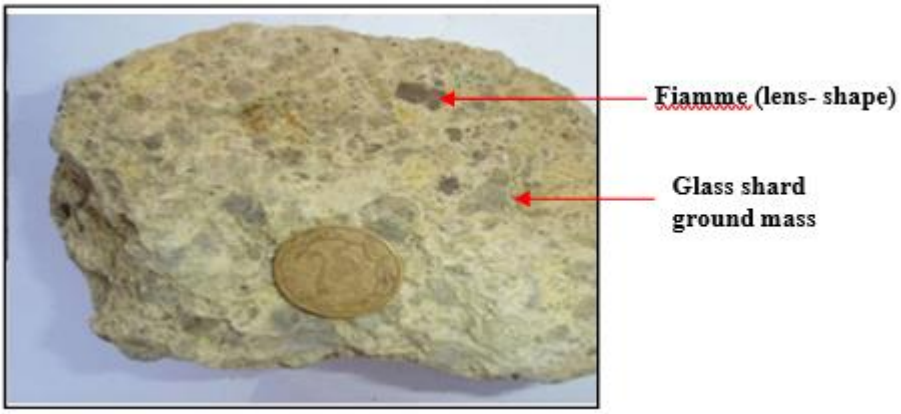


Fig .5: Ignimbrite rock sample

Rhyolite:

A common volcanic rock associated with basalts. They occured with dark to grey colours, with phenocrysts of quartz and alkali feldspars. Quartz in some ryholites was spheroidal indicating high temperatures of devitrification Fig .6.

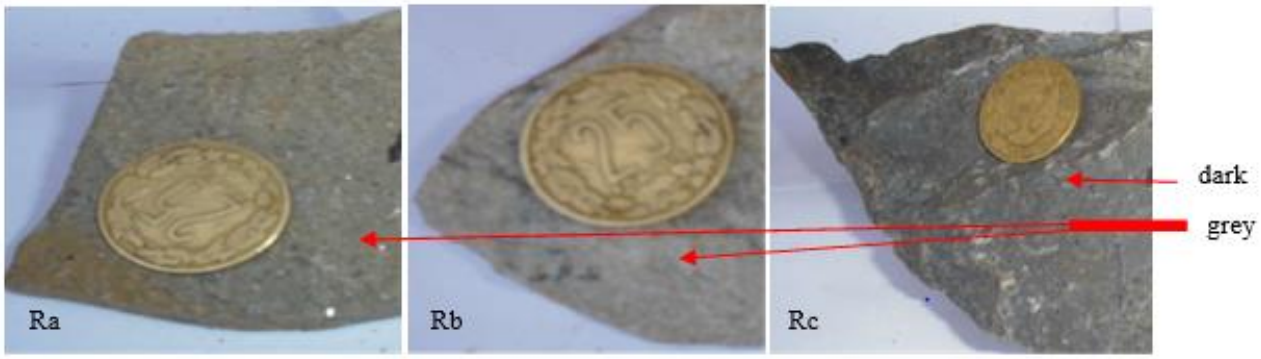


Fig .6: Rhyolite rock samples

Phonolite:

Phonolites had a white to grey colour, with an aphyric to porphyritic texture Fig .7.

Fig. 7: Phonolite rock sample

Scoria:

Identified within the Oku area associated to the volcanic activity responsible for the Oku massif.

It was an extrusive igneous rock of approximately 50% of silica having a vesiculartexture with a dark colour appearance having ellipsoidal vesicles (McPhie and Allen, 2005).

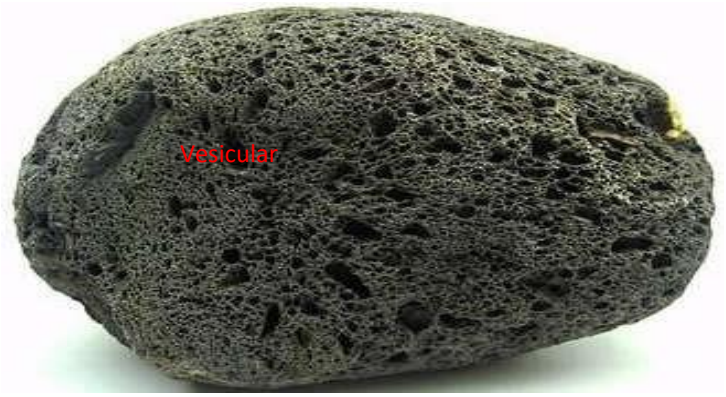


Fig .8: Scoria sample

Granites

Outcrops of the basement rocks occured within the locality of some water sources. Granites, Fig .9. constituted the basement complex on which the volcanic rocks overly, with outcrops at Ber, Mbam, Lip in Jakiri, Oku and Mbven subdivisions respectively. Also, there are outcrops along the banks of rivers that flow through Kumbo town. They were granular and phaneritic in texture with predominanlty whitish coloration, and often with pink to greyish colours depending on their mineralogy.

Fig .9: Granites sample Methods Laboratory analysis Petrographic analysis of the rock samples using Dave's method

Macroscopic appreciation of the rock samples was made. The basalts were from Kumbo, Nkum, Mbven, and Jakiri Subdivisions, with trachytes from Oku. The basalts were essentially porphyritic and aphyric in texture and covered approximately 80% of the study area with 4 out ofthe 5 samples being basaltic. Granites were sampled from Ber and Lip in Jakiri and Mbiame subdivisions respectively within the vicinity of boreholes studied. Seven thin rock section slides from basalts, trachytes, and granites from Bui were obtained. This was done in application of Dave's method on making thin sections (Hirsch, 2012). Thin sections of 0.03 mm (30 µm) thickness were prepared and attached on a glass slide with an epoxy and covered by another glass slide. Thin section slides of ignimbites, rhyolites, phonolites and scoria volcanic rocks commonly found associated with basalts and trachytes were used from Kamgang *et al*. (2008), at Bambui-Sabga area. A quantitative modal analysis was used to determine the volumetric proportions of the minerals

that made up some of the rocks determined by areal analysis of a thinsection. Point counting is a technique Whitney and Evans (2010) used by petrographers to get an approximate modal composition of rock from its thin section slide. The following steps were involved in the thin section slides preparations:

Step 1: Had as objective, to prepare a thin section with a constant thickness. The face of a glass slide was placed parallel to the face of the grinding wheel. The glass slide was ground to flatten it and roughen the surface for the epoxy to bind well. This was called a frosted glass slide that was placed in a slide holder. The grinding wheel was cleaned with a sponge and water. Waterwas poured on the wheel and dried with a paper towel.

Step 2: The rock sample was marked, to decide where to cut the rock. Generally, the thin section was cut in a plane perpendicular to a planar fabric on the rock.

Step 3: Cutting a slab, using a slab saw. The slab was cut from the rock along the line marked in step 2. Two cuts were made in parallel directions to obtain a slab, which was cleaned and allowed to dry.

Step 4: Part of the slab to be cut was decided and cutting the chip, reduced the size of the slab to slightly smaller than a thin section using a trim saw. Using a glass slide the correct size of the chip was determined using a diamond blade. The side of the chip from where the thin section will be made was polished to remove marks from the saw blade.

Step 5: Glue the slide to the chip. The frosted side of the slide was attached to the side of the chip that was just grounded down. The binding was by an epoxy ensuring a constant thickness across the section.

- The chip was heated up by placing it on one of hot plates with the polished side up for it not to get any dirt. This allowed the epoxy to flow easily and cure faster. Once the epoxy was well mixed, few drops were spread across the top (polished side) of the warmed chip. The epoxy was spread and waited until it soaked in 5 minutes, then more epoxy was spread. This was repeated until no more epoxy soaked into the chip.
- Sit to cure and check periodically for the first 5 to 10 minutes to be sure the slide has not slid off the chip. The epoxy cured in about 20 to 30 minutes (donot take the next step before that)

Step 6: Cutting off the chip from the slide was done as the rock chip was epoxied to the glass slide;

- This cutting off was done very slowly for it can break the slide.
- Once the chip was cut off the slide, the slide was rinsed to remove any particles.

Step 7: Grind the slide to correct thickness by grinding away rock remains but not all of it. This was the step in which most thin sections go bad. The key was to go slowly, especially near the end.

- The grinding wheel must be used carefully back and forth to evenly clean off the chip from the slide.
- Remove the slide and see if you can identify any minerals in the section. This was done and the process continued slowly until these minerals achieve the correct maximum

interference colour, for example quartz is pale yellow. We proceeded slowly especially when close to the correct thickness, for it was quite easy to go from slightly too thick to slightly too thin or ground completely away. In this study, a chemical analysis on the minerals was expected as such the section needed to be polished

- Caution was taken not to grind too fast for this could lead to cracking the minerals, the edges of the slide becoming thin and thick at the center. This was because these analysis tools require a flat, smooth surface at the micrometer scale.

Step 8: Place the slide-frosted side of a second glass section on the epoxy, and this serves as a cover slide. It is best to put one side down then let the other side fall to avoid trapping bubbles.

- Move the slide around with your finger or a pencil eraser. This squeezed out extra epoxy to achieve a constant thickness. The cover slide protects the section from damage

Step 9, required a cleaning up of the place where the thin slide preparation was carried out.

RESULTS

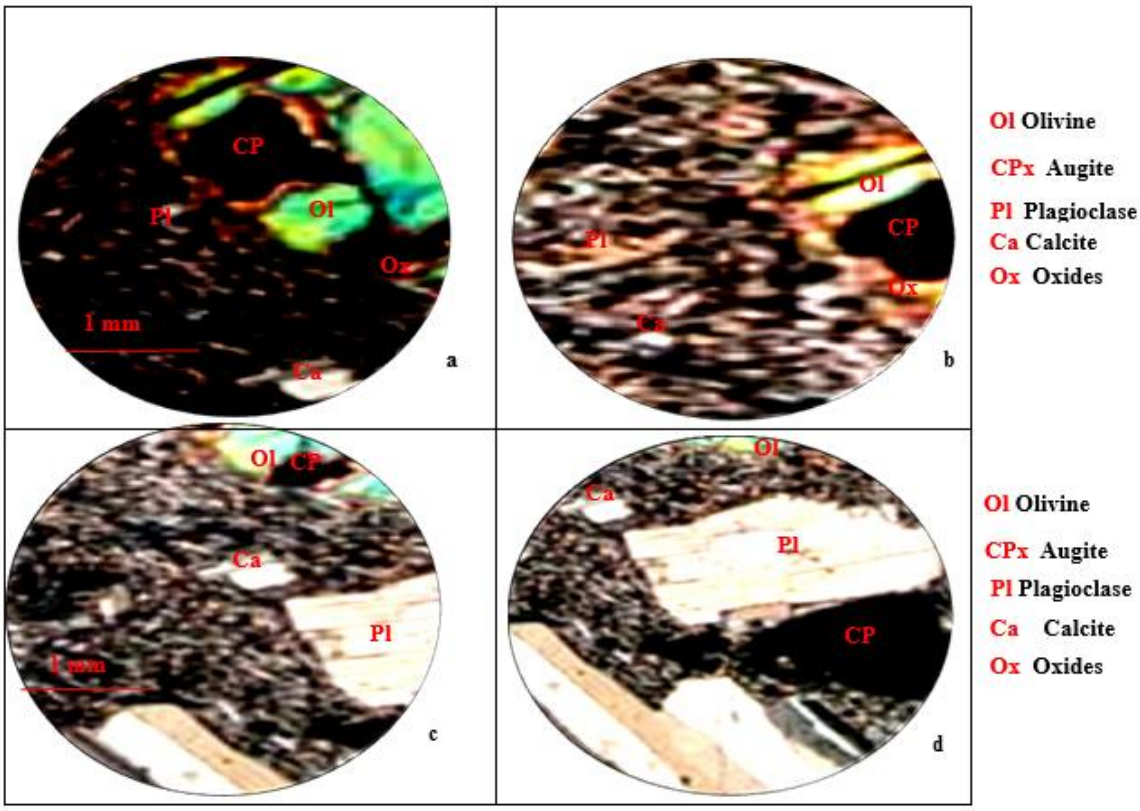
Thin Section Slides Observation of Porphyritic Basalts

This showed the presence of plagioclase, olivine, pyroxene and oxides of oxidized minerals in the groundmass. Plagioclase occupied about 70% of the total volume, with olivine, pyroxene and oxides making up the remaining 30% in the order: olivine > oxides > pyroxene;Fig .16(b). Table IV shows the modal (quantitative mineralogical) analysis of Bui basalts done inaccordance with (Chayes, 1967).

Table IV: Modal analysis of basalts

Basalt	**Minerals**	**MBI**	**BEL**	**NKA**	**YEH**
Phenocryst	Olivine	10	11	18	17
	Augite	1	1	9	10
	Plagioclase	2	2	--	--
	Total	13	14	27	27
Groundmass	Olivine	31	30	40	41
	Pyroxene	3	3	20	20
	Plagioclase	40	40	10	10
	Oxides	10	10	1	1
	Total	84	83	71	72
Total		97	97	98	99

Thin sections of the basalt observed under the Polarised Light Microscope (PLM); Fig.10revealed a preponderance of calcic plagioclase feldspars, pyroxene (augite) and olivine (forsterite). Calcite was also identified in the Bui basalts. Accessory minerals present were magnetite and ilmenite. The magnetite was present as phenocrysts in a groundmass of fine- grained feldspars. Both basalts (aphyric and porphyritic) were made of plagioclase microlites, microcrystals of oxides, olivine and clinopyroxenes scattered within the groundmass. Basalts overly most of the areas in Bui.



(a and b) Aphyric Basalt thin section (c and d) Porphyric Basalt thin section
Fig .10: Basalt thin sections (Under PLM)

Trachyte

The modal analysis of Bui trachytes met mainly in Oku Subdivision within the locality ofthe water catchment at Elak and the sampled river at Tolon were presented in Table V.

Table V: Modal analysis of trachyte

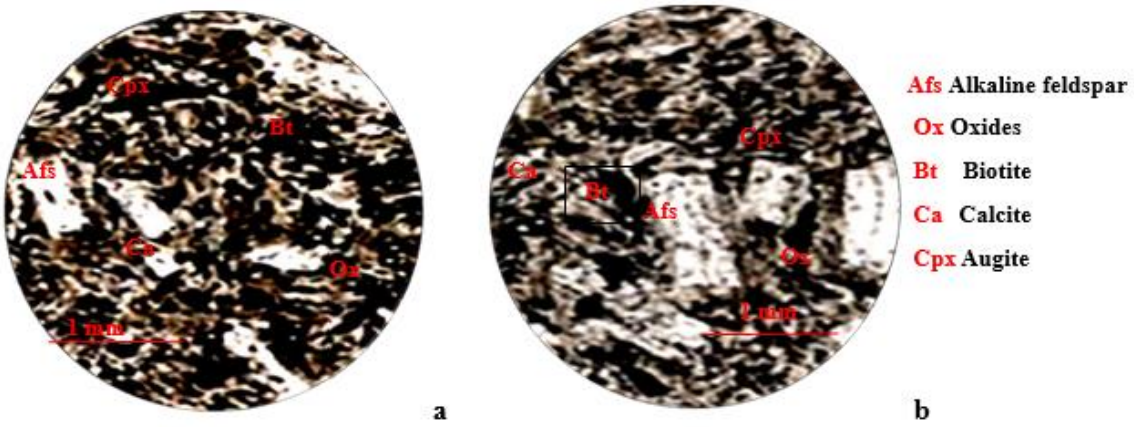
Trachyte	Mineral	ELA (Elak)	TOL (Tolon)
Phenocryst	Alkaline feldspar	22	20
	Oxides	15	15
	Calcite	18	19
	Biotite	5	5
	Total	60	59
Groundmass	Alkaline feldspar	15	15
	Oxides	06	05
	Calcite	12	13
	Biotite	4	5
	Total	37	38
Total		97	97

Thin Section Slide Observation of Trachyte

Thin section slide from trachyte; Fig .11 had as dominant mineral alkaline feldspars having large well shaped porphyritic crystals, and laths that form fine crystalline ground mass. They had elongated crystals of plagioclase with sanidine crystals, and clinopyroxenes mostly in the groundmass. The alkali feldspar was constituted of minerals that range from albite through

sanidine to orthoclase. Sanidine made up about 80% of the rock. Biotite, oxides and calcite constituted 20 % in the order; oxides > calcite > biotite. In addition to the dominantly clear

minerals, mafic minerals such as biotite, amphiboles (hornblende) and augite were identified. The mineral crystal sizes range from microcrystals to phenocrysts (0.25 ×0.5mm to 1.5 × 2.5mm). This agrees with works by (Flett, 1911).



(a)Trachyte thin section (Elak) (b) Trachyte thin section (Tolon)
Fig .11: Trachyte thin sections (Under PLM)

In addition to the basalts and trachytes which are dominant other associated volcanic rocks include: ignimbrites, rhyolites, phonolites and scoria whose study was done at Sabga in the Bamenda highlands by (Kamgang, 2003).

Thin Section Slide Observation of Ignimbrite
Vitroclastic texture with feldspar, quartz, plagioclase, pyroxene, oxides in Fig.12.

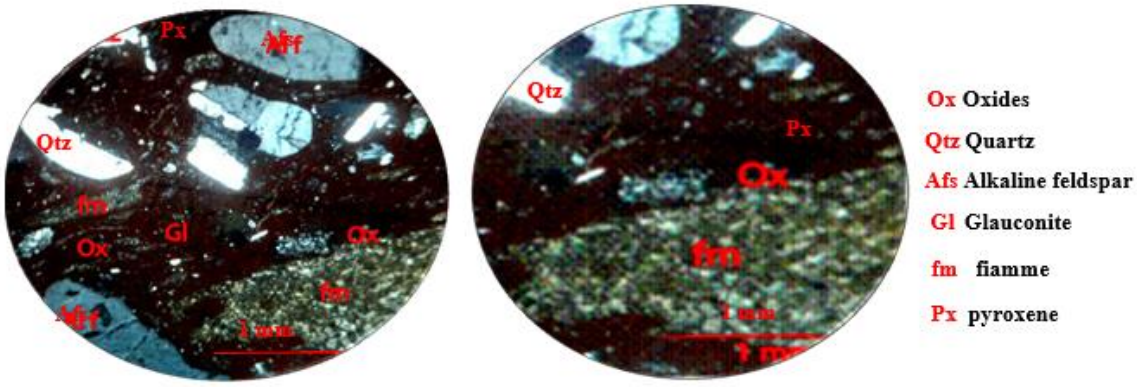


Fig .12: Thin section slides of ignimbrite from the Bambui-Sabga area.

Rhyolite
Modal analysis of rhyolites was presented in table VI. The minerals were in order quartz > sanidine > clinopyroxene. Rhyolite samples were presented in Fig .13.

Table VI: Modal analysis of rhyolite

Rhyolite	Minerals	Ra	Rb	Rc
Phenocrysts	Quartz	34	34	33
	Sanidine	16	17	15
	Clinopyroxene	03	02	03
	Plagioclase	05	06	09
	Oxides	02	01	03
	Total	60	60	63
	Quartz	25	25	20
Matrix	Sanidine	10	9	10
	Oxides	02	02	03
	Total	37	36	33
Total		100	100	

Thin Section Slide Observation of Rhyolites

The minerals present in rhyolite were mostly orthoclase (feldspars) with a ground mass composed of quartz, pyroxene, with the minerals occuring as isolated grains Fig .13. Quartz was most abundant and minerals were in order quartz (present as a phenocryst) > alkali feldspar > opaque oxides as inclusions in quatrz. Carlsbad twining was evident in sanidine crystals.

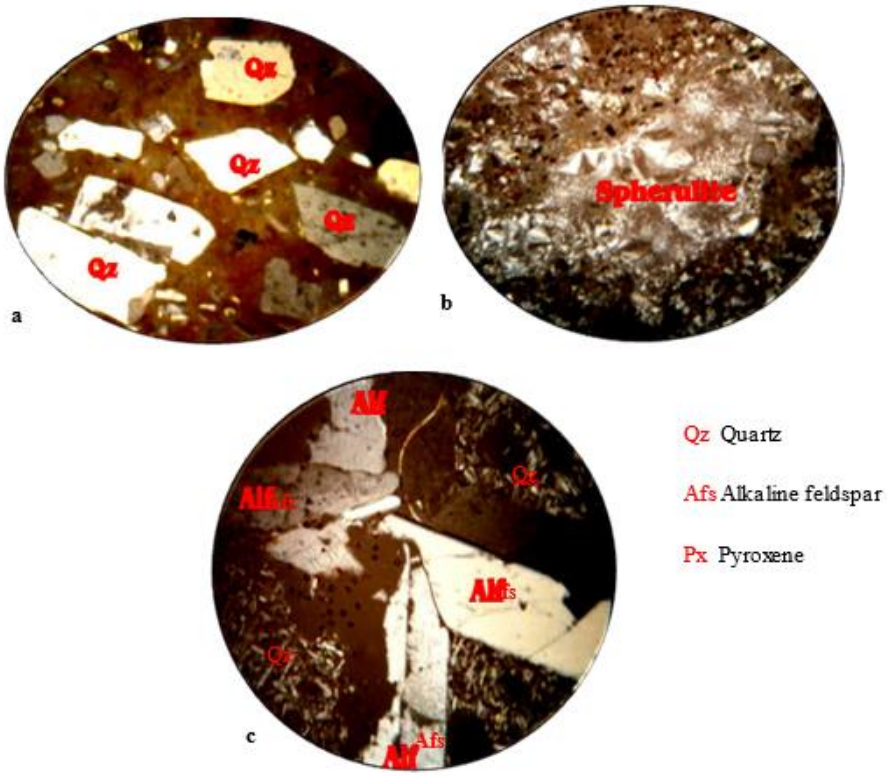


Fig .13: Thin section slide of Rhyolite from the Bambui-Sabga area; (a) Automorphic crystals of quartz, (b) Devitrification, (c) Sanidine showing twining.

Thin Section Slide Observation of Phonolite

The feldpathoids, alkaline feldspars and pyroxene were observed in order; feldspathoids (nepheline) > alkaline feldspars (sanidine) > pyroxene. Thin sections were presented in Fig .14.

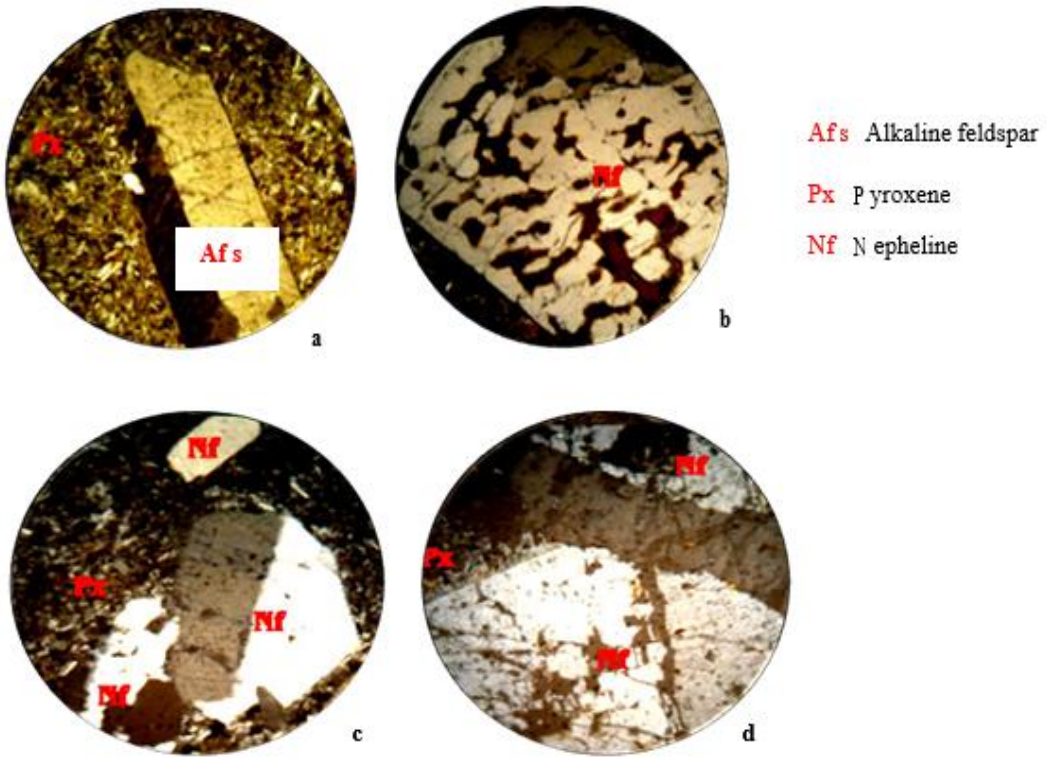


Fig .14: Phonolite thin section slides from the Bambui-Sabga area. (a) Sanidine phenocrysts, (b) Nepheline skeleton, (c and d) Nephelinecrystals.

Thin Section Slide Observation of Scoria

Thin section studies revealed scoria to be mainly hyalopilitic- porphyritic in textureassociated with a vitrophyric-porphyritic texture. Thin section slide in Fig .14 indicated sample was composed of phenocrystals of plagioclase. The major minerals were plagioclase and pyroxene. Minor minerals included apatite, biotite, haematite, hornblende, and magnetite.

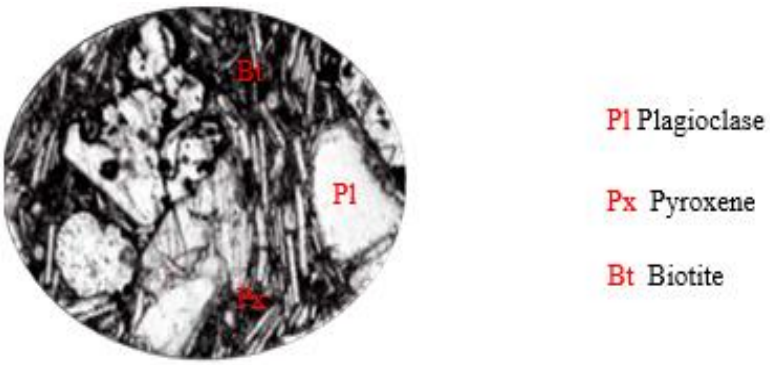


Fig .14 : Scoria thin section slide (PLM)

Granites

Thin Section Slide Observation:

The main minerals in thin section Fig.15 were quartz and alkali feldspars (orthoclase) with micas (biotite) and amphiboles as minor minerals. The alkali felspars constituted about 65 to 90 % of the total feldspar content in granites. On weathering most minerals undergo hydrolysis to form clay, and iron rich minerals oxidise to form the oxides. Micas (Muscovite)and quartz remain residual as they were resistant to weathering.

Fig .15: Granites sample thin section slide

The symbols of the minerals in the thin section slides were given in abbreviation form, (Whitney and Evans, 2010).

RESULTS OF THE PHYSICO-CHEMICAL PARAMETERS

The results of the physico- chemical parameters from the studied water samples in BuiDivision collected in 2016 and 2018 are presented in Table VII (a to f).

Table VII (a): Physico-chemical results of ground and surface water (n = 60) in Bui water catchments (February, May, August, November) in 2016; n = 40, and March/ September 2017; n = 20 (n = number of samples)

Catchment	ID	Alt	T	pH	EC	TDS	Na^+	K^+	Mg^{2+}	Ca^{2+}	Cl	HCO_3^-	SiO_2	SO^{2-}	NO_3^-	NH_4^+
		(m)	(° C)		µs/m		mg/l									
ELA 2016	ELA_1	2254	10.4	7.0	0.15	96.00	0.11	0.76	9.80	34.20	0.02	30.50	32.08	13.2	10.1	0.00
	ELA_2	2254	15.5	6.9	0.13	83.00	0.09	0.73	9.70	33.50	0.01	30.30	31.29	13.5	10.9	0.00
	ELA_3	2254	15.3	6.8	0.11	70.40	0.08	0.71	8.90	33.00	0.01	29.91	31.00	13.2	10.0	0.00
	ELA_4	2254	15.0	6.9	0.14	89.60	0.10	0.75	8.95	33.45	0.02	30.00	31.06	13.1	11.8	0.00
ELA 2017	ELA 1	2254	14.8	6.8	0.13	83.20	0.12	0.75	9.80	33.40	0.01	30.40	32.00	13.3	12.0	0.00
	ELA 2	2254	15.4	6.7	0.10	64.00	0.08	0.70	8.89	33.00	0.01	29.90	31.00	13.5	11.0	0.00
MBI 2016	MBI 1	2111	19.9	6.7	0.19	121.6	0.13	0.69	8.70	31.60	0.02	33.70	31.82	13.0	12.5	0.00
	MBI 2	2111	20.2	6.7	0.16	102.4	0.11	0.51	7.60	31.00	0.02	33.68	30.00	14.1	11.9	0.00
	MBI 3	2111	20.0	6.6	0.14	89.60	0.08	0.53	8.00	30.00	0.01	33.21	31.02	13.9	10.9	0.00
	MBI 4	2111	21.0	6.8	0.17	108.8	0.10	0.61	8.52	31.20	0.01	33.40	31.36	12.9	09.2	0.00
MBI 2017	MBI 1	2111	19.8	6.6	0.18	115.2	0.12	0.68	8.60	31.50	0.01	33.67	33.70	13.3	10.4	0.00
	MBI 2	2111	20.0	6.7	0.14	89.60	0.08	0.52	7.90	29.90	0.01	33.20	31.00	13.7	10.8	0.00
BEL 2016	BEL 1	2185	21.8	6.7	0.19	121.6	0.13	0.73	7.70	32.00	0.02	34.00	31.36	13.2	11.5	0.39
	BEL 2	2185	21.7	6.6	0.17	108.8	0.12	0.71	7.62	30.90	0.01	33.80	30.36	13.8	11.0	0.37
	BEL 3	2185	22.0	6.4	0.15	96.00	0.01	0.62	7.00	30.00	0.01	32.31	30.50	14.0	15.0	0.35
	BEL 4	2185	22.5	6.7	0.17	108.8	0.11	0.69	7.64	31.00	0.01	33.00	30.91	13.6	15.6	0.34
BEL 2017	BEL 1	2185	21.7	6.6	0.18	115.2	0.12	0.72	7.69	31.90	0.01	33.82	31.20	13.3	16.3	0.30
	BEL 2	2185	21.9	6.7	0.15	96.00	0.01	0.61	7.00	30.01	0.01	32.30	30.00	13.5	14.0	0.32
NKA 2016	NKA 1	1746	20.0	7.0	0.31	198.4	0.12	0.68	9.53	30.90	0.02	32.52	31.39	14.0	11.5	0.03
	NKA 2	1746	18.9	6.9	0.28	179.2	0.12	0.65	9.00	30.00	0.00	32.52	31.21	13.8	09.0	0.02
	NKA 3	1746	19.8	6.8	0.20	128.0	0.08	0.45	8.76	30.00	0.00	31.20	31.00	13.4	08.0	0.02
	NKA 4	1746	22.8	6.9	0.29	185.6	0.11	0.57	9.21	30.60	0.00	31.58	31.23	13.3	10.2	0.02
NKA 2017	NKA 1	1746	18.8	6.8	0.27	123.1	0.11	0.65	9.50	30.80	0.01	32.50	31.20	13.0	09.4	0.02
	NKA 2	1746	22.7	6.9	0.28	179.2	0.07	0.44	8.74	30.00	0.00	31.00	31.00	13.1	08.1	0.01
YEH	YEH 1	1895	21.0	7.1	0.30	192.0	0.14	0.13	9.21	40.20	0.02	33.60	31.82	14.0	10.0	0.00

2016	YEH $_2$	1895	20.5	7.0	0.22	140.8	0.13	1.00	9.00	39.90	0.01	33.54	31.03	13.9	10.8	0.00
	YEH $_3$	1895	20.6	6.7	0.20	128.0	0.11	0.08	8.52	37.82	0.01	31.50	31.00	13.2	10.1	0.00
	YEH $_4$	1895	22.9	6.8	0.28	179.2	0.12	0.09	8.80	38.54	0.01	32.30	31.40	13.6	10.0	0.00
YEH	YEH $_1$	1895	20.4	6.7	0.21	134.4	0.10	0.07	8.50	37.80	0.01	31.40	31.00	13.7	10.7	0.00
2017	YEH $_2$	1895	22.7	6.7	0.20	128.0	0.10	0.07	8.51	37.81	0.01	31.42	31.00	13.5	11.0	0.00
BEL	BEL_1	2185	21.8	6.7	0.19	121.6	0.13	0.73	7.70	32.00	0.02	34.00	31.36	13.2	11.5	0.39
2016	BEL_2	2185	21.7	6.6	0.17	108.8	0.12	0.71	7.62	30.90	0.01	33.80	30.36	13.8	11.0	0.37
	BEL_3	2185	22.0	6.4	0.15	96.00	0.01	0.62	7.00	30.00	0.01	32.31	30.50	14.0	15.0	0.35
	BEL_4	2185	22.5	6.7	0.17	108.8	0.11	0.69	7.64	31.00	0.01	33.00	30.91	13.6	15.6	0.34
BEL	BEL_1	2185	21.7	6.6	0.18	115.2	0.12	0.72	7.69	31.90	0.01	33.82	31.20	13.3	16.3	0.30
2017	BEL_2	2185	21.9	6.7	0.15	96.00	0.01	0.61	7.00	30.01	0.01	32.30	30.00	13.5	14.0	0.32
NKA	NKA_1	1746	20.0	7.0	0.31	198.4	0.12	0.68	9.53	30.90	0.02	32.52	31.39	14.0	11.5	0.03
2016	NKA_2	1746	18.9	6.9	0.28	179.2	0.12	0.65	9.00	30.00	0.00	32.52	31.21	13.8	09.0	0.02
	NKA_3	1746	19.8	6.8	0.20	128.0	0.08	0.45	8.76	30.00	0.00	31.20	31.00	13.4	08.0	0.02
	NKA_4	1746	22.8	6.9	0.29	185.6	0.11	0.57	9.21	30.60	0.00	31.58	31.23	13.3	10.2	0.02
NKA	NKA_1	1746	18.8	6.8	0.27	123.1	0.11	0.65	9.50	30.80	0.01	32.50	31.20	13.0	09.4	0.02
2017	NKA_2	1746	22.7	6.9	0.28	179.2	0.07	0.44	8.74	30.00	0.00	31.00	31.00	13.1	08.1	0.01
YEH	YEH_1	1895	21.0	7.1	0.30	192.0	0.14	0.13	9.21	40.20	0.02	33.60	31.82	14.0	10.0	0.00
2016	YEH_2	1895	20.5	7.0	0.22	140.8	0.13	1.00	9.00	39.90	0.01	33.54	31.03	13.9	10.8	0.00
	YEH_3	1895	20.6	6.7	0.20	128.0	0.11	0.08	8.52	37.82	0.01	31.50	31.00	13.2	10.1	0.00
	YEH_4	1895	22.9	6.8	0.28	179.2	0.12	0.09	8.80	38.54	0.01	32.30	31.40	13.6	10.0	0.00
YEH	YEH_1	1895	20.4	6.7	0.21	134.4	0.10	0.07	8.50	37.80	0.01	31.40	31.00	13.7	10.7	0.00
2017	YEH_2	1895	22.7	6.7	0.20	128.0	0.10	0.07	8.51	37.81	0.01	31.42	31.00	13.5	11.0	0.00

Table VII (b): Physico-chemical results of groundwater and surface water (n = 13) in Oku subdivision (1) (April/May 2018)

ID	Alt	Site	Depth	T	PH	EC	Na^+	K^+	Ca^{2+}	Mg^{2+}	HCO_3^-	NO_3^-	Cl^-	SO_4^{2-}	SiO_2
	M	(Name)	M	^oC		µs/cm	← mg/l →								
$BH1_a$	1388	GS Ibal	46	21.8	6.9	0.17	0.09	0.07	31.90	8.58	31.16	10.29	0.02	13.0	32.01
$BH1_b$	1808	CBC Jikijem	27	20.1	6.5	0.18	0.11	0.06	32.00	8.56	31.09	10.59	0.02	13.6	33.45
$BH1_c$	1837	GS Ichim	46	20,3	6.7	0.21	0.12	0.04	32.18	8.19	31.58	10.00	0.01	13.3	33.64
$BH1_d$	1347	GS Itoh Doh	46	20.9	6.8	0.15	0.09	0.05	33.00	8.50	33.69	10.09	0.01	13.7	32.18
$BH1_e$	1973	GS Ngashie	56	21.0	6.6	0.16	0.08	0.05	34.00	7.89	34.02	10.02	0.01	13.4	31.17
$BH1_f$	2048	CBC Ngvenkei	54	20.5	6.7	0.15	0.11	0.04	33.50	8.43	33.50	10.28	0.00	14.0	31.59
$ST1_a$	1764	Jikijem- Oku	---	20.8	6.9	0.18	0.13	0.05	33.61	8.57	32.58	11.45	0.00	14.0	33.00
$ST1_b$	1645	Ikal	---	20.3	6.8	0.17	0.15	0.08	32.91	9.00	31.90	11.08	0.02	14.1	32.50
$ST1_c$	1975	Elak	---	20.4	6.9	0.21	0.20	0.07	33.61	9.13	32.09	10.97	0.01	12.9	33.16
$RW1_a$	1632	Tolon	---	21.9	7.0	0.22	0.09	0.06	33.04	8.33	32.67	11.50	0.00	13.1	32.94
$RW1_b$	2050	Ngwenkie	---	21.7	6.7	0.21	0.08	0.07	32.95	8.56	31.88	11.08	0.00	13.9	32.93
$OW1_a$	1985	Catholic mission	23	21.4	6.6	0.17	0.13	0.06	32.82	8.48	31.78	10.62	0.01	13.7	32.19
$OW1_b$	1670	Oku Palace	20	21.1	6.7	0.20	0.14	0.05	32.79	8.50	32.00	11.10	0.01	14.0	32.00

OW: Open well. BH: Borehole. ST: Stream water. RW: River water. EC: Electrical conductivity. GS: Government school CBC: Cameroon Baptist Convention. CS: Catholic school. ID = Identity

Table VII (c): Physico-chemical parameters of groundwater and surface water (n = 9) in Mbven subdivision (2) (April/May 2018)

ID	Alt	Site	Depth	T	Ph	EC	Na^+	K^+	Ca^{2+}	Mg^{2+}	HCO_3^-	NO_3^-	Cl^-	SO_4^{2-}	SiO_2
	M	(Name)	M	°C		µs/cm	← mg/l →								
BH2a	1927	PS Rifem	65	22.2	6.9	0.18	0.10	0.06	31.99	8.72	32.92	10.00	0.01	13.0	33.25
BH2b	1919	GS Rifem	45	23.0	7.0	0.16	0.11	0.04	31.98	7.97	33.52	10.20	0.02	13.8	33.58
BH2c	1904	CS Rifem	55	22.8	6.6	0.15	0.09	0.05	32.00	8.88	33.55	11.06	0.01	13.4	33.43
BH2d	1740	GS Sang	80	23.3	6.8	0.17	0.12	0.08	32.51	8.92	34.01	11.04	0.00	13.1	32.91
BH2e	785	GS Lip	45	24.5	6.9	0.20	0.13	0.06	32.08	8.31	33.95	10.09	0.01	13.7	32.01
ST2	1940	Kitang	---	23.1	6.7	0.15	0.08	0.08	33.00	8.00	31.90	10.50	0.01	12.9	32.82
RW2	1960	Mbven	---	23.0	6.5	0.14	0.14	0.07	32.91	7.98	31.00	10.34	0.01	14.1	32.19
OW2a	1936	Mbiame market	10	23.7	6.8	0.22	0.13	0.05	34.00	8.54	32.74	10.19	0.00	13.5	33.70
OW2b	1938	Mbiame market	12	23.6	6.9	0.23	0.11	0.06	33.81	8.96	32.19	11.00	0.00	13.9	33.52

PS: Presbyterian School ID: Identity

Table VII (d): Physico-chemical parameters of groundwater and surface water (n =12) in Nkum subdivision (3) (April/May 2018)

ID	Alt	Site	Depth	T	Ph	EC	Na^+	K^+	Ca^{2+}	Mg^{2+}	HCO_3^-	NO_3^-	Cl^-	SO_4^{2-}	SiO_2
	M	(Name)	M	°C		µs/cm	← mg/l →								
BH3a	2027	GS Tatum	42	21-9	6.5	0.16	0.10	0.06	32.97	8	31.98	10.18	0.02	13.9	31.92
BH3b	2060	IPS Tatum	36	21.7	6.6	0.13	0.14	0.08	33.01	7.89	32.29	10.37	0.00	14.0	31.58
BH3c	2048	CS Tatum	34	21.6	6.8	0.18	0.12	0.04	33.26	8.79	32.38	10.45	0.00	14.1	31.69
BH3d	2185	PS Mah	32	21.8	7.0	0.15	0.08	0.07	32.15	8.19	32.18	11.50	0.01	13.1	31.00
BH3e	2182	IPS Takijah	30	21.9	6.7	0.15	0.11	0.05	32.13	8.11	33.69	10.85	0.02	13.8	32.93
BH3f	2158	CS Dzeng	28	21.8	6.5	0.16	0.12	0.06	31.99	8.13	33.00	10.64	0.00	13.5	33.00
ST3a	1888	Memfu	---	22.0	6.9	0.17	0.11	0.07	32.06	8.56	34.02	11.19	0.00	13.3	33.60
ST3b	1891	Memfu	---	22.1	6.8	0.16	0.12	0.06	32.18	8.33	34.00	11.05	0.00	12.9	33.65
RW3	1892	Mbi-im	---	22.3	6.9	0.20	0.08	0.08	33.98	7.94	33.17	10.50	0.02	13.0	32.96
OW3a	2028	Hill top hotel	24	21.0	7.0	0.21	0.13	0.07	34.01	8.00	33.39	10.00	0.01	13.7	31.99
OW3b	2005	Tatum market	19	21.2	6.6	0.19	0.09	0.06	34.00	8.03	33.79	10.02	0.02	13.7	31.90
ST3c	1991	Memfu road	---	22.4	6.7	0.16	0.10	0.05	34.11	8.14	33.68	11.11	0.02	13.2	31.16

Table VII (e): Physico-chemical parameters of groundwater and surface water (n =15) in Jakiri subdivision (4) (April/May2018)

ID	Alt	Site	Depth	T	Ph	EC	Na^+	K^+	Ca^{2+}	Mg^{2+}	HCO_3^-	NO_3^-	Cl^-	SO_4^{2-}	SiO_2
	M	(Name)	M	°C		µs/cm	← mg/l →								
$BH4_a$	1201	GS Wasi	48	24.0	6.6	0.16	0.11	0.06	33.21	7.95	31.20	10.10	0.00	12.9	31.00
$BH4_b$	1552	GS Tan	55	23.6	6.8	0.18	0.13	0.08	32.32	8.25	31.00	10.50	0.01	13.1	32.01
$BH4_c$	1424	GS Kwanso	50	23.4	6.5	0.20	0.09	0.04	32.10	8.33	31.24	11.00	0.01	13.4	33.50
$BH4_e$	1695	CS Jakiri	65	24.1	6.7	0.13	0.12	0.06	33.01	8.41	31.15	11.12	0.02	13.2	33.61
$BH4_f$	2071	IPS Fakuiy	30	22.6	6.6	0.14	0.13	0.07	33.24	7.99	31.99	11.05	0.01	14.0	33.24
$BH4_g$	2051	GS Vekovi	59	23.8	6.9	0.19	0.08	0.05	32.91	7.69	32.00	10.98	0.00	13.9	31.50
$ST4_a$	1670	Wahrin	----	21.0	6.4	0.21	0.07	0.07	32.80	8.36	32.01	10.00	0.01	14.1	31.14
$ST4_b$	1671	Vet school	----	20.9	6.8	0.15	0.10	0.06	32.80	8.00	33.40	10.20	0.01	13.2	33.50
$ST4_c$	1673	Nsulong	----	20.1	6.8	0.16	0.12	0.04	34.00	8.12	33.12	11.11	0.02	13.7	33.19
$RW4_a$	1748	Sop (Kiree)	----	21.9	6.7	0.14	0.11	0.08	34.01	8.15	31.99	11.45	0.00	13.3	33.70
$RW4_b$	1629	Mensai	----	22.5	6.6	0.22	0.13	0.05	33.03	8.98	32.16	10.50	0.00	13.1	32.50
$RW4_c$	1674	Tsemkan upper	----	22.3	70	0.21	0.14	0.06	32.91	8.00	33.43	10.45	0.01	14.0	32.51
$RW4_d$	1636	Tsemkan lower	----	22.9	69	0.16	0.12	0.04	32.08	8.57	33.17	10.51	0.02	14.0	33.00
$OW4_a$	1600	Abakwa	----	22.3	68	0.15	0.13	0.04	32.63	8.60	33.24	10.00	0.02	13.1	32.59
$OW4_b$	1612	St Jude's Clinic	----	22.1	67	0.17	0.11	0.05	33.34	8.17	32.18	10.61	0.01	13.8	32.19

Table VII (f): Physico-chemical parameters of groundwater and surface water (n =28) in Kumbo subdivision (5) of Bui (April/May2018)

ID	Alt	Site	Depth	T	pH	EC	Na^+	K^+	Ca^{2+}	Mg^{2+}	HCO_3^-	NO_3^-	Cl^-	SO_4^{2-}	SiO_2
	M	(Name)	m	°C		µs/cm	◄ mg/l ►								
$OW5_a$	1613	Komban street	1.0	21.0	5.9	0.21	0.10	0.09	34.20	8.50	31.42	11.0	0.02	12.9	32.00
$OW5_b$	1654	Tobin Mosque	46	19.9	6.5	0.19	0.13	0.06	33.96	8.62	32.00	10.9	0.01	13.0	31.00
$OW5_c$	1721	CS Tobin	48	20.9	6.8	0.23	0.11	0.08	33.92	8.91	33.21	10.6	0.01	13.3	32.90
$OW5_d$	1734	Catholic Univ	50	20.0	6.7	0.18	0.11	0.06	34.00	7.90	33.00	11.2	0.01	13.1	31.36
$OW5_e$	1845	SAC	36	19.8	6.5	0.24	0.10	0.07	32.91	8.02	31.19	11.3	0.02	13.8	33.70
$OW5_f$	1916	Bamkikaiy	4	20.2	6.0	0.22	0.14	0.10	32.98	8.52	31.00	11.2	0.00	13.6	32.10
$OW5_g$	1946	LAP Centrek'bo	15	21.2	5.9	0.20	0.12	0.09	34.00	8.53	31.20	10.8	0.01	13.9	32.00
$OW5_h$	1922	Pig farm Bamkikaiy	19	21.1	6.8	0.17	0.13	0.09	34.03	8.51	31.00	10.3	0.01	14.0	33.00
$ST5_a$	1695	Meluf upper	----	20.0	6.7	0.19	0.11	0.08	34.11	8.50	32.00	11.0	0.01	14.4	32.10
$ST5_b$	1671	Meluf lower	----	21.0	6.8	0.18	0.10	0.09	33.97	7.92	33.21	10.9	0.01	13.2	31.90
$ST5_c$	1665	Roh Bui upper	----	19.7	6.7	0.20	0.12	0.08	33.06	8.25	30.21	11.4	0.02	13.5	31.87
$ST5_d$	1646	Roh Bui lower	----	19.9	6.5	0.22	0.14	0.06	33.08	8.50	32.11	11.2	0.01	12.9	32.00
$ST5_e$	1874	Roh Kimbo up	----	20.0	6.6	0.16	0.11	0.07	32.91	8.51	33.40	10.8	0.01	13.1	32.01
$ST5_f$	1633	Roh Kimbo low	----	21.1	6.9	0.18	0.10	0.08	31.90	8.53	33.20	10.5	0.01	13.0	32.03
$RW5_a$	1687	Meluf	----	19.9	6.5	0.21	0.13	0.08	34.11	8.10	31.00	10.1	0.00	13.0	32.82
$RW5_b$	1620	Roh Bui	----	19.8	6.7	0.20	0.10	0.09	34.00	8.23	33.40	10.0	0.02	13.7	31.00
$RW5_c$	1615	Meluf/ Bui	----	20.0	6.6	0.22	0.13	0.08	34.30	8.25	32.00	10.2	0.02	12.9	31.57
$RW5_d$	1610	Roh Kimbo	----	21.0	6.8	0.19	0.14	0.07	33.90	8.51	31.19	11.5	0.02	13.4	32.50
$RW5_e$	1604	Bui/Roh Kimbo	----	21.0	6.7	0.17	0.11	0.09	32.98	8.50	31.20	11.2	0.01	13.9	31.92
$RW5_f$	1900	Romajaiy	----	21.2	6.6	0.23	0.10	0.10	33.21	8.52	32.00	10.9	0.01	14.0	30.90
$RW5_g$	1876	Nji-iy	----	20.0	6.5	0.20	0.13	0.07	34.00	8.51	32.18	10.0	0.02	12.9	31.80
$RW5_h$	1860	Kinsaan	----	19.9	6.8	0.21	0.14	0.08	34.12	8.00	31.16	10.5	0.02	13.3	31.70
$BH5_a$	1906	GS Bamkikaiy	31	21.2	6.8	0.24	0.12	0.06	33.91	8.60	31.40	10.9	0.00	13.1	33.40
$BH5_b$	2020	CBC Kishiy	35	22.3	6.6	0.22	0.11	0.08	33.70	7.98	30.92	11.2	0.02	13.9	32.98
$BH5_c$	1763	GS Kiyan	50	22.0	6.7	0.20	0.10	0.05	32.91	8.51	31.20	11.0	0.01	12.9	31.82
$BH5_d$	2037	GS Tadu	55	21.9	6.5	0.24	0.14	0.07	33.00	8.20	29.90	11.4	0.02	13.0	32.60
$BH5_e$	1968	GS Kai	45	22.2	6.7	0.20	0.11	0.06	33.10	8.25	30.00	10.6	0.02	14.0	31.90
$BH5_f$	1742	GS Njavnyuy	65	23.0	6.6	0.18	0.13	0.08	33.69	7.99	31.25	10.8	0.01	13.5	32.00

GS= Government school. CS= Catholic school. LAP= Life abundant programme. SAC= Saint Augustine's Colle

DISCUSSION AND INTERPRETATION

Dissolution of Minerals from Rock Samples

The dissolution of the minerals can be presented in form of chemical equations. The ions in water were responsible for the various analysis to depict suitability for different purposes as well as classify water from the sources. Many authors have published works that support the dissolution of rock minerals as the basis of controlling water quality (Gibb's, 1970; Tardy, 1971; Sarin *et al.*, 1989; Schott *et al*., 1989; Schweda, 1989; Njilah, 1991; Frogner and Schweda, 1998; Srinivasamoorthy *et al.*, 2008; Xiang *et al.*, 2008; Yuce *et al*., 2009; Kengni *et al*., 2011; Temgoua 2011; Tay, 2012; Mengnjo *et al*., 2013). Based on the mineralogy of the rock samples viewed in thin sections the following equations are written;

$$CaCO_3\ (s) + H^+\ (aq) + HCO_3^-\ (aq) \longrightarrow Ca^{2+}\ (aq) + 2HCO_3^-\ (aq) \quad \text{..... (1)}$$

Calcite

$$Fe_2SiO_4(s) + 4H_2CO_3\ (aq) \longrightarrow 2Fe^{2+}\ (aq) + 4HCO_3^-\ (aq) + H_4SiO_4\ (aq) \quad \text{.....(2)}$$

Olivine

In the presence of oxygen, the dissolved iron is quickly converted to haematite with a perception of iron oxides in the slides.

$$2Fe^{2+}\ (aq) + 4HCO_3^-\ (aq) + 1/2O_2\ (g) + 2H_2O\ (l) \qquad Fe_2O_3(s) + 4H_2CO_3\ (aq) \quad \text{.....(3)}$$

Pyroxenes, amphiboles and olivines are most susceptible to oxidation because of their high iron content. Iron contained in the minerals combines with oxygen and water to form hydrated iron oxides.

$$4Fe^{2+}\ (aq) + 3O_2\ (g) + 6H_2O\ (l) \qquad 2(Fe_2O_3.\ 3H_2O)\ (s) \quad \text{.....(4)}$$

Anorthite and albite end members of the plagioclase minerals present in the rock minerals.

$$3CaAl_3Si_5O_{16} + 8CO_2 + 9H_2O \longrightarrow 3Ca^{2+} + 6HCO_3^- + 4SiO_2 + 3AlSi_2(OH)_4 + 2CO_2 \text{..... (5)}$$

Anorthite

(Anorthite - Albite). Reactions that characterize hydrochemical evolution of groundwater in plagioclase dominated rocks.

$$2NaCaAl_3Si_5O_{16} + 8CO_2 + 9H_2O \longrightarrow 2Ca^{2+} + Na^+ + 6HCO_3^- + 4SiO_2 + 3AlSi_2(OH)_4 + CO_2 \text{.....(6)}$$

$$2KFe_3AlSi_2O_{10}(OH)_2 + 13H^+ + CO_2 + 2H_2O \blacktriangleright Al_2SiO_5(OH)_4 + 4H_4SiO_4 + 2K^+ + 6Fe^{3+} + HCO_3^- \text{.....(7)}$$

Biotite

The variations observed in the water samples from the different water bodies were greatlydue to the rocktypes of the environments and to a limited extent human activity within the vicinity of the water bodies.

The Hydrochemical Facies

The concentrations of major ion analysis from all sampling sites revealed the Ca^{2+}, Mg^{2+} and HCO_3^- as the dominant species. The lower concentration of K^+ in the water samples was due to its low geochemical mobility (Hem, 1989; Srinivasamoorthy *et al*., 2008). These variations in concentrations of major ions were represented with Bar charts in Fig. 56 for each water catchments in 2016. Fig. 57 illustrated a graphical representation for other water sources during the different expeditions in 2018.

In all data, the ions had the highest concentrations in the dry season and the lowest concentrations in the rainy season within the water catchments. The high concentrations were found in the heart of the dry season in February, while low concentrations were observed in August at the peak of the rainy season. This could be because during the rainy season, much rain results in the dilution of the ions, unlike the dry season with no dilution. This agrees with the factthat the climatic conditions could influence the water chemistry of the water samples (Kiming *et al*., 2020a, 2020b).

The high prevalence of the nitrate ion was observed at the Belem catchment (BEL) where animal rearing was done within the open unprotected plain of the catchment and at ELA due to animal rearing at the summit of Oku Mountain that would result in the infiltration of urine and faecal desposits. A high prevalence of nitrates and sulphate ions was observed within the rivers that flow through Kumbo because of farming within the flood plains of these rivers with regular application of some fertilizer. Equally, runoff of wastes from homes, garages, slaughter houses and a prison could also enhance the prevalence. The major ions relevant to the Piper diagram presented in Table VIII, were used to determine the hydrochemical facies (water type) of the Bui water catchments studied, OW, BH, ST and RW in this work.

Table VIII: Percentages of cations and anions for classification (Piper, 1994)

Sites	$Na^+ + K^+$	Ca^{2+}	Mg^{2+}	HCO^-	SO^{2-}	Cl^-
ELA	1.90	75.70	21.40	68.50	30.20	0.04
MBI	1.70	77.60	20.70	71.20	28.70	0.03
BEL	1.90	76.60	19.00	73.90	29.20	0.04
NKA	1.80	75.60	22.70	73.80	26.10	0.04
YEH	1.00	80.60	18.30	70.20	29.90	0.07
OW	0.50	79.40	20.20	72.90	27.10	0.01
BH	0.40	79.50	20.10	70.30	29.70	0.02
ST	0.50	79.20	20.30	70.40	29.80	0.02
RW	0.40	79.30	20.20	70.30	29.50	0.02

Variations in mg/l for major ions (Na^+, K^+, Mg^{2+}, Ca^{2+}, Cl^-, HCO_3^-, NO_3^-, SiO_2) in the water catchments were illustrated in a Bar chart in Fig. 16.

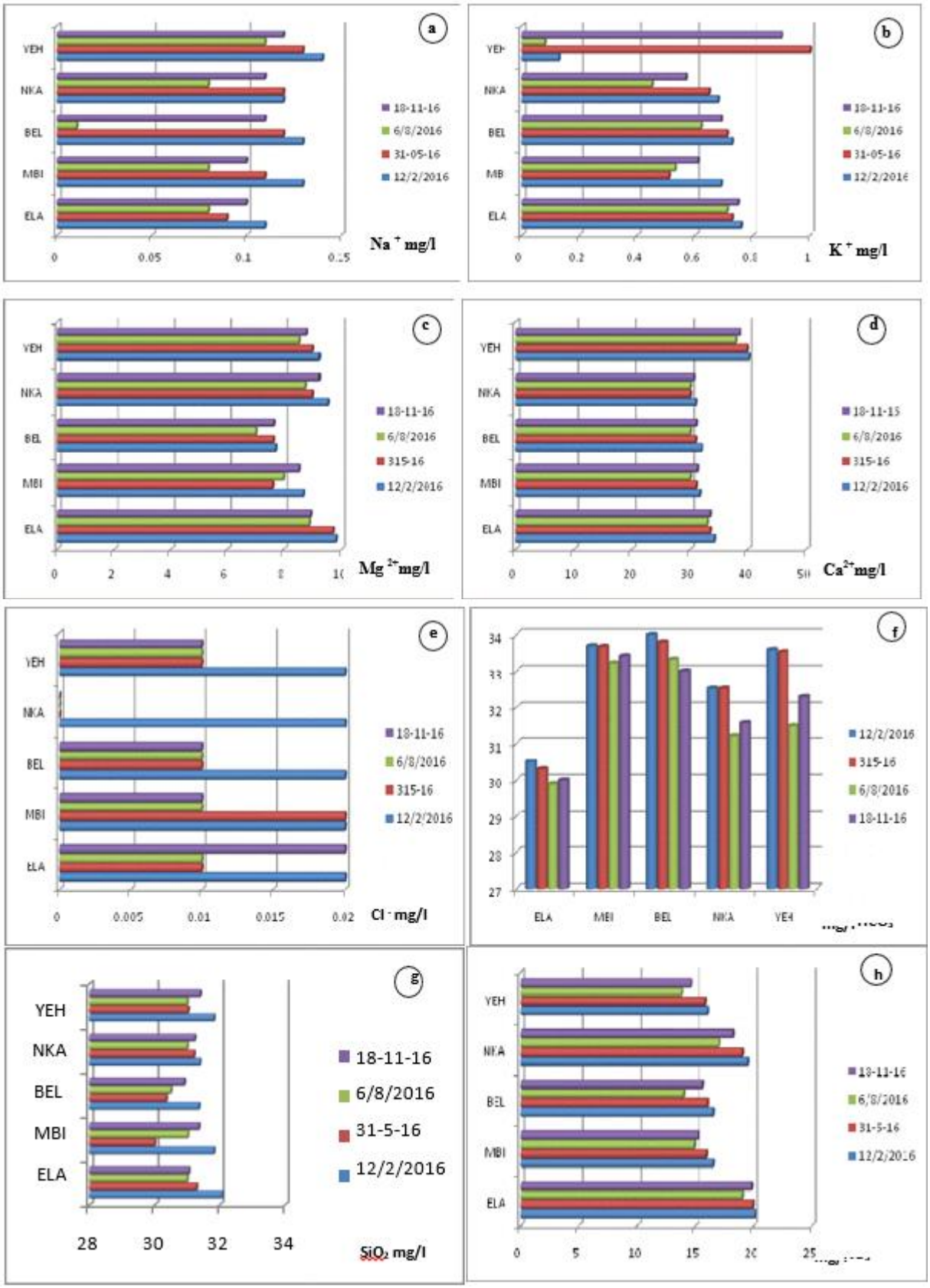


Fig. 16: Variations of the major ion concentrations in the Bui water catchments in 2016

In open wells, boreholes, streams and rivers the dominance of Ca^{2+} and HCO_3^- over all the other ions was evident with a significant contribution in boreholes. The variations in concentrations of these ions determined in 2018, presented in Fig. 17; again, confirmed the

dominance of Ca^{2+} and HCO_3^-. mg/l

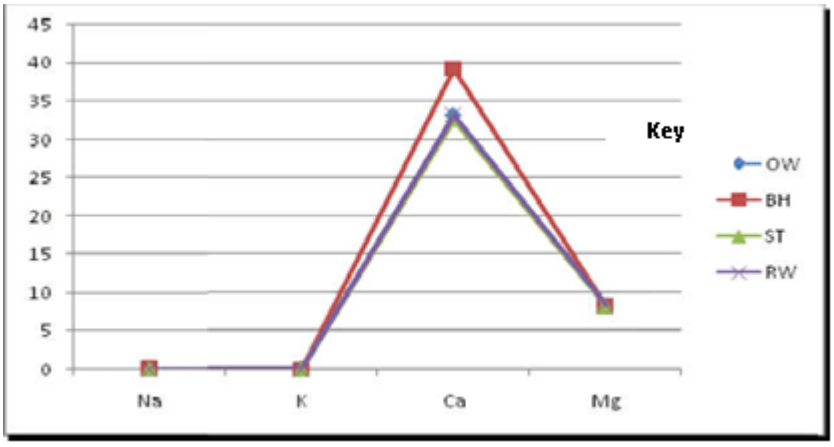


Fig.17: Variations of the major ion concentrations in OW, BH, ST and RW

Water Classification Piper Diagram

The water classification enabled the water types of the study area to be obtained.The Piper diagram; Fig. 18 determine the water type, wherein most samples plotted in the alkalineearth metals and bicarbonate domains. This indicated the dominance of alkaline earth metals in the aquifer systems. From the percentages calculated and presented in Table VIII, a general chemical nature of the water was observed by plotting major cation and anion concentrations ona Piper tri-linear diagram, (Piper, 1944). The Bui water catchments and OW, BH, ST and RW were dominantly the calcium bicarbonate water types; $Ca(HCO_3)_2$.

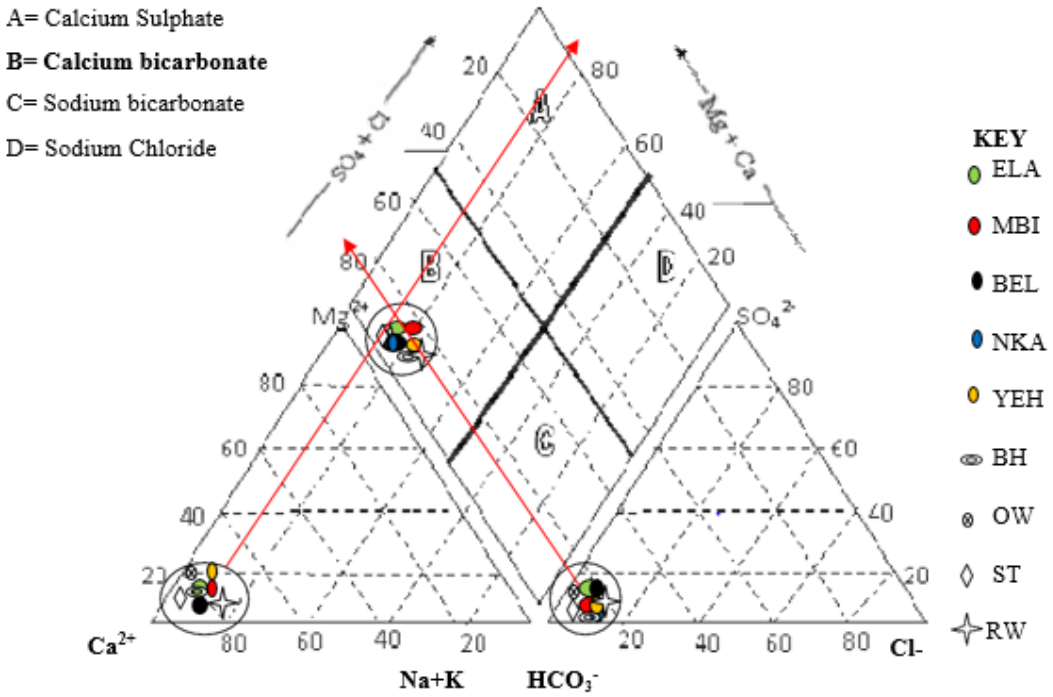


Fig.18: Water types and hydrochemical facies (Piper,1994)

The percentage of HCO3- was very high compared to other anions, while Ca2+ was the dominant cation. The observation prevailed in all the water sources during the different expeditions.

GENERAL CONCLUSION

In all water sources in our study sites same as elsewhere, the mineralization of the water sources has both anthropogenic and natural sources. In this research it is clearly expressed that; despite the two main sources of water mineralization, the dissolution of primary minerals from the rock samples is the dominant process responsible for mineralization. This is further supported by the dissolution of the different silicate minerals into the water sources as evident in the different chemical reactions for the dissolution of these minerals. Nonetheless, influence of chemical fertilizers in water mineralization could be possible in areas with large scale uses that could be verified in Bui division within the vicinities of commercial gardening. a perspective set for verification.

Perspectives

The water mineralization of water sources is dominantly a natural process governed by the dissolution of rock minerals. Agricultural practices within the vicinity of some water sources particularly in some neighborhoods with commercial gardening could have a high prevalence of NO_3-, K+, $SO_4$2- and $PO_4$3- due to a considerable application of Nitrates, potassium, sulphate and phosphate fertilizers. This perception could be verified in areas having commercial gardening activities prevalent to discern the influence of fertilizers in the ions derived from application of specific chemical fertlizers

Acknowledgements

This article is part of a PhD research by the corresponding author, in the department of Earth science of the faculty of science in the University of Dschang. Laboratory analysis were done in St Anne's Physicochemical and Biomedical laboratory in New Bell Douala. Provision of the HI 83200 Multiparameter Bench photometer, manufactured by Hanna instruments Inc in the Highland industrial park of the United States of America for physico- chemical parameter analysis was quite innovative, efficient and rendered analysis within extremely minimal error margins. Thin rock sections permitted identification of minerals whose dissolution reactions were presented in form of chemical equations for releases of ions into water.

Conflict of Interest

No conflict of interests was witnessed in the execution of this research in which the authors had absolute collaboration and support from the Earth science department of the University of Dschang and the College of Technology of the university of Bamenda

Data Availability

A totality of the data used in the development of this article that includes the physico- chemical and petrographic data are available in this article.

REFERENCES

Akoachere, R. A., Eyong, T.A., Egbe, S.E., Wotany, R.E., Nwude, M.O and Yaya, O.O (2019). Geogenic Imprint on Groundwater and Its Quality in Parts of the Mamfe Basin, Manyu Division, Cameroon. Journal of Geoscience and Environmental Protection, 7, 184-211. https://doi.org/10.4236/gep.2019.75016.

Akoachere, R.A., Yaya, O.O., Egbe, S.E., Eyong, T.A., Nji, B.N., and Tambe, D.B. (2019). GIS-Hydrogeochemical Model of the Yaounde Fractured Rock Aquifer, Cameroon: Aquifer setting, Seasonal Variations and Water Quality. Journal of Geoscience and Environmental Protection, 7, 232- 263 https://doi.org/10.4236/gep.2019. 75018.

Appelo, C. A. J. and Postma, D. (2005). Geochemistry, groundwater and pollution (2nd edition). Balkama, Amsterdam p 635.

Chayes, F. (1967). Modal compositions of U.S.G.S reference sample G-2. Geochim.

Cosmochim. Acta, V.13, pp. 463- 464.

Dechao, C., Acef, E., Hualian, X., Xinliang, X., and Zhi, O. (2020). A Study in the Relationship between Land Use Change and Water Quality of the Mitidja watershed in Algeria Based on GIS and RS. Sustainable Water Quality Management in the Changing Environment 2020. 12(9), 3510; htpps:// doi. Org/10.3390 su 12093510.

Deutsch, W. J. (1997). Groundwater geochemistry. Fundamentals and applications to contamination. CRC Press. Florida p221.

Edmunds, W. M and Smedley, P. L. (1996). Ground water geochemistry and health with reference to developing countries. Geological Society Special Publication No. 113 pp 91-105.

Flett, T. S. (1911). Trachyte.In Chisholm, Hugh (ed). Cambridge University Press. Pp.166-117. Fondzenyuy.V.F and Kengni.L. (2021). Hydrogeochemistry of alternative water sources in Bui division, North west region of Cameroon: Implications on drinking, domestic and agricultural uses. PhD Thesis, University of Dschang, Faculty of sciences, department of Earth sciences 2021

Frogner, P. and Schweda, P. (1998). Hornblende dissolution kinetics at 25 degrees C. In the geochemistry of crustal fluids. Vol. 151 (ed. K. V. Ragnarsdottir and E.H (Oelkers) pp169-179. Elsevier.

Frommen, T., Groeschke, M., Noelscher, M. & Schneider, M. (2019) Anthropogenic and geogenic impacts on peri-urban aquifers in India – Insight from a Case Study in the Northeast of Jaipur (in prep.)

Germain, K.N.G., Jules, M.O.M., Narcisse, K.A., Aristide, G.D., et Lanciné, D.G. (2019). Caractérisation hydrogéochimique des eaux souterraines du bassin versant de la Baya, Est Côte d'Ivoire. International Journal of Biological and Chemical Sciences, 13(1): DOI: https://dx.org/10.4314.v13i1.44

Gibbs, (1970). Mechanisms Controlling World Water Chemistry. Science 170, 1088- 1090. Hirsch Dave. (2012). How to make a thin section. https:// Davehirsch.com/other/ thin sections. Inam, E., Inoh, G.G., Offiong, N.O., and Etim, B.B. (2017). Physico-cheomical Characteristics and Health Risk Assessment of Drinking Water Sources in Okoroette Community, Eastern Coast of Nigeria. American Journal of Water Resources, vol.5, no.1,pp.13- 23.2017.

Kamgang, P. (2003). Pétrologie et géochimie d'un secteur clé de la ligne du Cameroun ; les Monts Bamenda ; implication sur la genèse et l'évolution des magmas. Thèse de Doct. D'Etat Ydé I. P373+ annexe.

Kengni, L., Tematio, P., Kuitcha, D., and Manefouet, B. (2006). Water balance and hydrochemical behaviour of experimental catchment in the West Cameroon highlands Ann Fac. Sc. Univ. Ydé I, Vol. 36, n°3, pp.47-63.

Kim, J. G., Ko, K. S., Kim, T. H., Lee, G. H., Song, Y., Chon, C. M., and Lee, J. S. (2007).

Effect of mining and geology on the chemistry of stream water and sediment in a small watershed. Geoscience Journal, 11, 175- 183.

Kiming, I.N., Godwill, T.N., Moye, E.K, (2020a). Climate Variability Impact and Adaptation: The Experience of Maize Farmers in Bui Division, Northwest Cameroon. International Journal of Environment, Agriculture and Biotechnology, 5(3) May-Jun 2020/https:// ijeab,com/.

Kiming, I.N., Moye, E.K., Jude, K, (2020b). Mountain Agriculture and Environmental Dynamics: Impact of Climate Variability in Bee Farming in Oku, Cameroon. International Journal of Environmental Sustainability and Soil Science, 1(1), 77-87, https://doi.org/10.388142/ ijesss,

McPhie, J. M. D and Allen, R. (2005). Volcanic Texture. A guide to the interpretation of textures in volcanic rocks Centre for Ore Deposit and Exploration Studies, University of Tasmania, Hobart, Tasmania pp 198.

Mengnjo, J. W., Takeshi, O., Wilson, Y. F. Samuel, N. A., Justice, Y. S., Asobo, N. E. A., Gregory, T., and Joseph, V. H. (2013). Hydrochemistry of shallow ground water and surface water in the Ndop plain, North West Cameroon. African Journal of Environmental science and Technology. Vol 7.

Mohammed, H., Yangun, S., Mohamed, M., Weijin, J., Majid, K., and Qiang, G. (2020). Assessment of Groundwater Resources in Coastal Areas of Pakistan for Sustainable Water Quality Management Using Joint Geophysical and Geotechnical Approach : A Case Study. Sustainable Water Quality Management in the Changing Environment 2020. 12(22), 9730 ; https://doi.org/10.3390/su 12229730.

Ngako, V., Affaton, P., and Njonfang, E. (2008). Pan-African tectonic in North–Western Cameroon implication for history of Western Gondwana. Gondwana Res 14; 509- 522.

Njilah, I. K., Temdjim, R., Nzolang, R. C., Ghogomu, R. C., Tchuitchou, C., Rose, H. N., and Ajonina, H. N. (2007). Geochemistry of tertiary- quaternary lavas of Mount Oku, North West Cameroon. Revista Facultad de Ingenieria. 40: 59-75.

Njoyim, E.B.T., Mofor, N.A., Niba, M.L.F., and Sunjo, J. (2016 a). Physicochemical and bacteriological quality assessment of the Bambui Community drinking water in the North West Region of Cameroon. African Journal of Enviromental Science and Technology, vol. 10, no, 6, pp. 181- 191, 2016.

Njoyim, E.B.T., Biosengazeh, N.F., Alakeh, M.N, Tameu, D.Y. (2016 b). Quality control of domestic water in Babessi village in North West in Cameroon. International Journal of Biological and Chemical Sciences, 10(3): 1382-1402.

Piper, A. M. (1944). A graphic procedure in the geochemical interpretation of water analysis.

Trans Am. Geophys. Un papers. Hydrol, pp 914 – 629.

Richard, A.E., Chris, F., and Dane, V. (1987). Weathering of Basalts, Changes in Rock chemistry and mineralogy. Clay and Minerals, vol 35. No 3, 161-169.

Sajil, K, P.J., Elango, L., James, E.J. (2014) "Assessment of Hydrochemistry and water quality in south Chennai coastal area". Arabian Journal of Geosciences 7:2641–2653

Sajil, K, P. J., Davis, D. P., James, E.J. (2014) "Groundwater chemistry and its implications on suitability for irrigation purposes in Vaniyambadi and Vellore Taluk, South India". National Academy Science Letters 37 (6): 493-502

Sarin, M. M., Krishnaswami, S., Killi, K., Somayajulu, B. L. K., and Moore, W. S. (1989). Major ion chemistry of the Ganga–Brahmaputra River basin system: weathering processes and fluxes to the Bay of Bengal. Geochimica et Cosmochimica Acta, 53, 997– 1009.

Schott, J., Brantley, S. L., Crerar, D. A., Guy C., Borcsik, M., and Willaime, C. (1989). Dissolution kinetics of strained calcite. Geochimica and Cosmochimica Acta, 53 (2), pp. 373-382.

Schweda, P. (1989). Kinetics of alkali feldspar dissolution at low temperature. In water-rock interactions; WRI-6., Vol. 6 (ed. D. L. Miles), pp.609-612. International Association of Geochemistry and Cosmochemistry and Alberta research council, sub-group on Water- rock interaction.

Srinivasamoorthy, K., Chidambaram, S., Prasanna, M. V., Vasanthavihar, M., Peter J., and Anandhan, P. (2008). Identification of major sources controlling groundwater chemistry from a hard rock terrain. A case study from Meltur taluk, Salem district, Tamil Nadu. J. Earth Syst, Sci 117: 49-58.

Tanyileke, G. Z., Kusakabe., and Evans, W. C. (1996). Chemical and isotopic characteristics of fluids along the Cameroon Volcanic Line pp 433-441.

Tay, C.K. (2012). Hydrochemistry of groundwater in the Savelugu-Nanton District, Northern Ghana. Environ Earth Sci. 67:2077-2087.

Temgoua, E. (2011). Chemical and bacteriological analysis of drinking water from alternative sources in the Dschang Municipality, Cameroon. Journal of Environmental Protection Vol.2 No.5.

Tyagi, S., Singh, P., Sharma, B., and Singh, B, (2014). Asseeement of Water Quality for Drinking Purposes in District Pauri of Uttarakhand, India. Applied Ecology and Environmental Sciences, vol.2,no.4,pp. 94-99, 2014.

WHO. (2017). Guidelines for Drinking- Water Quality. 4th Edition. Incorporating the First Addendum, Geneva.

WHO. (2018). Developing drinking-water quality regulations and standards. Water sanitation hygiene. Publication on water sanitation and health.

WHO. (2019). UN-Water Global Analyses and Assessment of Sanitation and Drinking-Water (GLASS) 2019 Report.

Whiteney, D. L and Evans, B. W. (2010). See; American Mineralogist, Volume 95, pp 185- 187.

Whitten, D. G. A. and Brooks, J. R. V. (1978). A Dictionary of Geology. Penguin books, pp 494- 511.

Xiang, H., Mika, S., Bu, D., Egil, T., and Gjessing. (2008). Water quality in the Tibetan Plateau: Metal contents of four selected rivers. Environmental Pollution 156, 270-277.

Yuce, G., Ugurluogha, D., Dilaver, A. T., Eser, T., Sayin, M., Donmez, M., Ozcelik, S., and Aydin, F. (2009). The effects of lithology on water pollution; Natural radioactivity and trace elements in water resources of Eskisehir Region (Turkey).Water, Air and Soil Pollution, 202, 69-89.