An Assessment of the Impact of Cocoa Flavonoid on Health

¹Afnan Alsulimani, ²Saddiga Al-Ghalib, ³Amal Elyas

Abstract--The birthplaces of chocolate are exceptionally old, followed back to the Maya people, who were most likely the first to develop the cacao plant, in 400 AD. Chocolate comes from cocoa beans, the fruit of the cacao tree or the scientific name Theobroma. Chocolate has important healthy properties. Organic dark chocolate with a high percentage of cocoa seeds or flavonoid (70% and more) can have an impact on the cognitive functions, and prevent age related neurodegeneration and cognitive declines in memory and learning, especially for elder people. Flavonoids can clash neuronal injury that can cause neurodegenerative disorders such as Alzheimer and Parkinson disorders. Also, flavonoids can be preventive to some chronic diseases such as cardiovascular and diabetes, because it has an extended variety of biological impacts. Therefore this study identifies the impact of cocoa flavonoid on health through review study and the finding shows that consuming average amounts regularly is the main key to benefit the brain functions.

Keywords--Healthy Effects; Cocoa; Chocolate; Flavonoids; Memory; Cognitive Functions; Alzheimer; Cardiovascular; Insulin Resistance; Dementia

I. INTRODUCTION

Chocolate came to Europe in the 16th century. Since then, the modern chocolate industry has developed, and cocoa seeds are now processed in different ways [1].Chocolate is the most commonly craved food in the world [2]. Chocolate did become a favourite confection in most developed countries including Europe and North America. Nowadays cocoa is grown mainly in West Africa, Indonesia, and Sri Lanka [1]. The consumption of chocolate as a confection is widespread in most developed countries, with consumption being highest in Europe and the United States [3].

The origins of chocolate are very old, usually traced back to the Maya people, who were probably the first to cultivate the cacao plant, in 400 AD [4]. The word cacao is derived from Olmec and the subsequent Mayan languages (kakaw). Early colonial era documents included instructions for the medicinal use of cacao [5]. Cacao originated and grew up in the new world and spread to Europe in the middle of the sixteenth century, it was used medicinally as a basic treatment and as a link to deliver other medicines [6].Cocoa and chocolate are different from each other; chocolate originates in cocoa beans, the fruit of the cacao plant. Through different processing, cocoa and chocolate are derived from the seeds of the cacao tree or Theobroma cacao- its scientific name [7].

¹College of Humanities, Effat University, An Nazlah Al Yamaniyyah, Jeddah 22332, Saudi Arabia. E-mail: aaalsulimani@effatuniversity.edu.sa ²College of Humanities, Effat University, An Nazlah Al Yamaniyyah, Jeddah 22332, Saudi Arabia. E-mail: salghalib@effatuniversity.edu.sa ³College of Humanities, Effat University, An Nazlah Al Yamaniyyah, Jeddah 22332, Saudi Arabia. E-mail: aelyas@effatuniversity.edu.sa

Due to its health effects, in the past, it was considered the drink of Gods [8]. A scientific association assigned a scientific name to the cocoa tree "Theobroma cacao"; which refers to the Greek word Theo (God) and Broma (drink) [1]. Cacao tree are rich in a subclass of polyphenol antioxidants known as flavonoids, specifically catechin and epicatechin, as well as polymeric units which comprise bothcatechin and epicatechin subunits, both are collectively referred to as proanthocyanidins (orprocyanidins) [9, 10]. Flavonoids are a set of natural elements with variable phenolic structures found in plantsand it has been consumed by humans for about 4 million years [11]. The best results were found using 71% and above of cocoa dark chocolate [12].

In 1930 a new element was isolated from oranges. At that time researches believed it could be a member of a new element of vitamins and was named as vitamin P. Later on it became clear that this element was a flavonoid up to date more than 4000 varieties of flavonoidshave been found [13]. Flavonoids that are natural bioactive plant compounds found in foods such as tea, cocoa and fruits [14]. It was found that the consumption of foods rich in flavonoid leads to neurological effects in improving aspects of learning, memory, and general cognitive performance [15]. Other health effects were noticed in populations with high consumption of cocoa.

Kuna Indians of the San Blas islands of Panama have one of the lowest prevalence of hypertension (2.2%). They also experience a lower rate of blood pressure as they aged. In addition, the rate of diabetes mellitus, myocardial infarction and cancers is lower compared to mainland Panamanians. It was suggested that the reason of better health rates is due to high intake of the Kuna Indians population of cocoa beverage as reported by Katz et al. [16].Therefore this study identifies the impact of cocoa flavonoid on health through review study.

II. METHODOLOGY

The information gathering process was done through searching on various sites on the internet such as using Google scholars, Science Direct, PubMed, PMC and this searches was conducted between October 2017 and April 2018, using search terms to search for pertinent resources: In title:(Internet, online, journals articles and web site) to identify randomized controlled trialsexamining the effect of cocoa flavonoids on brain and memory. All searches were limited to fulltext, in English papers, Furthermore, searched bibliographic citations from review articles. Which have been peer reviewed, were published up to 2017.These searches showed over748,000 results. Science direct, PubMed and Google scholar were searched using the term "cocoa flavonoid, Alzheimer disease, dementia, cardiovascular disease, memory" (major subject heading). The researches were selected according to recent studies and its validity.

III. LITERATURE REVIEW

Memory in psychology has been divided into three different processes: encoding, storage and retrieval [17]. According to McDermott [18], "Encoding is defined as an initial learning of information; storage refers to maintaining information over time; retrieval is the ability to access information". Diseases such as Alzheimer, Parkinson and Dementia can negatively impact memory that leads to a decrease in cognitive abilities which weaken daily activities [19]. Patients with dementia suffer from deteriorating life style that affects their health and family

relations significantly. People who are taking care of such patients' usually face daily challenges. Therefore, improving patients' memory is highly needed.

There are some studies that examine certain techniques to improve memory. According to Glizer[20], cognitive training has shown some short term improvement in part of the cognitive function in Parkinson's patient. Several studies had worked in cognitive rehabilitation technique for Alzheimer disease, including cognitive stimulation by a discussion focusing on repeatedly reminding the patient of information using themes and cognitive training for practice of task designed to exercise a specific cognitive function [21]. Another technique being used for improving memory includes sleeping, meditation and healthy diet. There is a considerable interest in the possibility of phyto chemicals to increase memory and general cognitive ability [22]. When the person intake of chocolate the flavonoid elements absorbed to access and accumulate in the brain area that is responsible in learning and memory, especially in the hippocampus [23].Vauzouret al. [24]found that the impact of flavonoid on cognitive function was associated with the ability of flavonoids to interact with cellular and molecular models responsible for learning and memory. Furthermore, cocoa flavanols can protect, manage and improve regular cognitive functioning performance [25].

Healthy individual's intake of cocoa increases their cerebral blood flow [26]. These flavonoids increase blood flow to the brain, which promote the formation of new neurons, improve nerve cell function, and protect neurons from death [10]. Cocoa flavonoid has an effect in reducing cerebral cases like dementia, stroke and cognitive decline. Also it improves blood pressure and insulin levels [27]. Daily consumption of dark chocolate reduces the possibility of a stroke attack [28]. It has also a positive impact on improving the cognitive performance of older people who are suffering low memory decline, in addition to an increase of their verbal fluency [29]. Cocoa flavanols consumption has been examined in older people with early memory decline and it was found that the cognitive performance was improved by a daily intake of cocoa flavanols for 8 weeks [30]. The study conducted by Socci et al. [25], compared between low-flavanol participants (48 mg) with high-flavanol participants (993 mg) usage of 8 weeks. The result indicated that higher cocoa flavonoid is associated with obvious more improvements in mental function, memory, and verbal fluency compared to the low flavanol group. Also, similar findings in young, healthy participants showed that daily consumption of high flavonoids within 8 weeks increased their cognitive performance [25].

Neurotransmitters that contain flavonoids elements through some procedures have the ability to protect neurons at risk and stimulate nerve functions through interaction with signalling pathways between neurons [22]. The flavonoids are considered to effect cognitive function by influencing the signalling pathways that are involved in normal memory processing [15]. Theobroma cacao has shown beneficial effects on memory and learning. These studies clearly established the efficacy of flavonoid foods in enhancing cognitive performance. They fall short of providing evidence that flavonoids are the causal agents in driving a favourable effect on memory [31]. A strong evidence that flavonoid intake has a positive impact on the cognitive function.

A study was conducted by Spencer [22], on a total of 1640 participants who are not suffering from dementia aged 65 and above. The study focuses on the cognitive performance with different tests by taking their

academic level, gender and age into consideration for 10 years. The participants were divided into two groups; first group had an intake of (mg/d; 13.60–17.69 and 17.70–36.94) of cocoa flavonoid.

It was found to have led to an improvement in their cognitive development more than the second group in with (0–10.39 mg/d). After 10 years of the study, "participants with the lowest flavonoid intake were found to have lost about 2.1 in the examination score, however, participants with the highest amount had lost only 1.2points" [22]. The study indicated that flavonoid intake is fundamentally associated with positive and better cognitive performance over time.

Flavonoid and health benefit

Food rich in flavonoids considered to be of highest benefit to the human health. It can be found in different sources such as chocolate, raspberries, and citrus fruit, red wine, and tea [32]. According to Yao et al. [33], "Flavonoids are naturally the phenolic antioxidants that are present in the human diet". Several clinical investigations conducted over the past two decades have shown that food rich in flavonoids has a positive effect on long term health, and can relieve many chronic diseases [34]. Flavonoids usually contain antioxidants, which exhibit a protective role against several systemic illnesses such as cardiovascular disease, cancer, Alzheimer and dementia [33].

Cardiovascular Disease

Lifestyle modification, including healthy diet has been established as one of the most important factors that can significantly influence the incidence of cardiovascular disease [35]. Dietary flavonoid had a favourable impact on inflammation and vascular homeostasis [36]. Buijsse et al [37] was first to report the relationship between cocoa consumption and reduced blood pressure in the Zutphen Elderly Study. Several studies have similar results, however, other studies have no significant changes in blood pressure linked with use of cocoa products containing regular levels of flavanols, the majority of the research conducted in this area indicated that regular cocoa/ chocolate ingestion can decrease blood pressure.

One study conducted by Prasain [38] showed the positive correlation between flavonoid and reduction of cardiovascular disease, confirmed that both genders of participants who use high amounts of flavonoids had 18% lower risk of cardiovascular diseases compared to those who did not have enough high amount.

Effects on Insulin Resistance

Insulin resistance may be attenuated by flavanols through reducing oxidative stress, improving endothelial function, and/or altering glucose metabolism. Ceriello and Motz [39] have "proposed that oxidative stress is the underlying mechanism for both insulin resistance and cardiovascular disease".

Alzheimer Disease

Alzheimer disease is a debilitating disease that leads to progressive deterioration of cognitive brain function, leaving its victim almost dependent on their caregivers. Dementia is the primary manifestation of the

disease [40]. According to Gill et al. [41], "Alzheimer's disease is the sixth leading cause of death in the US". There are an increasing number of studies related to phytochemical foods to prevent neurodegeneration and cognitive decline. Latest evidence has shown that flavonoids can have an effect on a person's cognition and may increase memory and learning levels [42,45].

A Norwegian study has been conducted by Nehlig [10] on 2031 participants in their 70's to measure the impact of flavonoids from cocoa and other resources on cognitive performance. Findings showed that those who used cocoa flavonoid did better in the cognitive examination than those who did not.

Flavonoids effect can be connected with cognitive protection as we age. Flavonoids taken from different food sources have a stronger effect. The consumption of diet containing large amounts of food rich with flavonoid by elderly is linked to better performance in many cognitive abilities [43]. Alzheimer is neuronal injury, flavonoids can prevent these damages through their interaction with signalling proteins in the pathways that protect the alive ones [44].

Critical Analysis

Nehlig[10] has recently conducted an experiment on flavonoids on mice, he was able to prove that it can decrease age related cognitive damage. However, they these results support the critical role of flavonoids in resisting or limiting cognitive decline as well as the prevention of neurological diseases during aging. Nurk et al. [43], reported improvement of cognitive performance as a result of large amounts of some flavonoid intake. It was associated with better performance in several cognitive abilities. Another concern is the effect of food processing techniques of cocoa on the natural content, Latif [1] mentioned in his article that the products used in studies often contain much higher flavonoid contents than most of the commercially available products. Industrialists have created processing techniques for cocoa to exclude the bitterness all together, since flavonoids have a bitter taste. 90% of the flavonoids might be gone because of cocoa processing. Thus, it needs to be established whether the consumption of products with lower flavonoids content is associated with any health benefits in humans [12,46]. Pimentel et al. [12] mentioned in his study that the best results were found using 71% and above of cocoa dark chocolate. Reviewing the studies on the flavonoid use of health protection needs to be critically assessed in reference to the dose used in those studies.

IV. DISCUSSION

Management of chronic illnesses has been dependent on the use of medications for a long period of time. In recent years the interest in other modalities of treatment became more widely used, i.e. natural, herbal medicine and dietary products. According to the studies in this literature review, dark chocolate is one of the richest sources of flavonoids elements. That leaves milk chocolate in a lower level of importance as per the studies. White chocolates have no role whatsoever. Dark chocolate has important healthy properties. Flavonoids have an effect on cognitive brain function such as memory. Eating cocoa regularly can improve mental capacity. Chocolate and cocoa helped to improve a range of health problems dating back to antiquity, as chocolate benefits cardiovascular, neurological and behavioural function. Cocoa flavonoids, caffeine and the bromine, improve mental performance and skills. Since

flavonoids have positive effects on the brain, mental abilities and memory improvement, flavonoids can therefore protect the body against Alzheimer's disease, stroke and dementia. Cocoa daily intake for 8 weeks offers a high level of protection for the elderly people against the cognitive decline that leads to dementia, while among young healthy people it increases the general cognitive of function. Cardiovascular disease is a major health issue all over the world. Any protective component is of a great value. As we have discussed, it seems that flavonoids has a beneficial effect on the cardiovascular system by improving risk factors as blood pressure and insulin resistance. Although this research has given some insight on the subject many aspects are still not clear.

V. CONCLUSION

In conclusion, the interest of the impact of food on human health has been increased recently. Pointing to the fact that flavonoid cocoa is one of the interesting elements proposed to protect human cognition. This literature review major goal was to evaluate whether cacao or its constituents are capable of improving memory and cognitive function. The findings were that cocoa flavonoids found to be effective in protecting different type of cognitive function such as the memory, increasing the cognitive performance, attention and learning. Choosing either organic dark chocolate with a high percentage of cocoa seeds or flavonoid 70% or more can affect the brain positively because it contains phytochemicals, methylxanthines and flavonoids. Consuming average amounts regularly is the main key to benefit the brain functions.

VI. ACKNOWLEDGMENTS

The authors would like to thank to College of Sciences and Humanities, Effat University for their unconditional support.

REFERENCES

- 1. Latif, R. 2013. Chocolate/cocoa and human health: a review. *Neth J Med.* 71, 2, 63-8.
- 2. Weingarten, H. P. and Elston, D. 1991. Food cravings in a college population. *Appetite*. 17, 3, 167-175.
- 3. Fold, N. 2001. Restructuring of the European chocolate industry and its impact on cocoa production in West Africa. *Journal of Economic Geography*. 1, 4, 405-420.
- 4. Verna, R. 2013. The history and science of chocolate. *Malaysian J Pathol 2013*. 35, 2, 111-121.
- 5. Dillinger, T., Barriga, P., Escárcega, S., Jimenez, M., Lowe, D. and Grivetti, L. 2000. Food of the Gods: Cure for Humanity? A Cultural History of the Medicinal and Ritual Use of Chocolate. *The Journal of Nutrition*. 130, 8, 2057S-2072S.
- 6. Lippi, D. 2009. Chocolate and medicine: Dangerous liaisons?.*Nutrition*. 25, 11, 1100-1103.
- Kelishadi MD, R. 2005. Cacao to Cocoa to Chocolate: Healthy Food?.*ARYA Journal 2005 (Spring)*. 1, 1, 28-34.
- 8. Shah hirva, pateljenisha (2016) bicelle: a lipid nanostructure for transdermal delivery. Journal of Critical Reviews, 3 (2), 17-22.
- 9. Dillinger, T. L., Barriga, P., Escárcega, S., Jimenez, M., Lowe, D. S. and Grivetti, L. E. 2000. Food of the gods: cure for humanity? A cultural history of the medicinal and ritual use of chocolate. *The Journal of nutrition*. 130, 8, 2057S-2072S.
- 10. Steinberg, F. M., Bearden, M. M. and Keen, C. L. 2003. Cocoa and chocolate flavonoids: implications for cardiovascular health. *Journal of the American dietetic association*. 103, 2, 215-223.
- 11. Nehlig, A. 2013. The neuroprotective effects of cocoa flavanol and its influence on cognitive performance. *British journal of clinical pharmacology*. 75, 3, 716-727.
- 12. Kumar, S. and Pandey, A. K. 2013. Chemistry and biological activities of flavonoids: an overview. The Scientific World Journal. 2013, 1-16.

- 13. Pimentel, F. A., Nitzke, J. A., Klipel, C. B. and de Jong, E. V. 2010. Chocolate and red wine–A comparison between flavonoids content. *Food Chemistry*. 120, 1, 109-112.
- 14. Middleton, E. 1998. Effect of plant flavonoids on immune and inflammatory cell function. In Flavonoids in the living system. Springer, Boston, MA.175-182
- 15. Ross, J. A. and Kasum, C. M. 2002. Dietary flavonoids: bioavailability, metabolic effects, and safety. *Annual review of nutrition*. 22, 1, 19-34.
- 16. Patel DM, Jani RH, Patel CN. "Ufasomes: A Vesicular Drug Delivery." Systematic Reviews in Pharmacy 2.2 (2011), 72-78. Print. doi:10.4103/0975-8453.86290
- 17. Letenneur, L., Proust-Lima, C., Le Gouge, A., Dartigues, J. F. and Barberger-Gateau, P. 2007. Flavonoid intake and cognitive decline over a 10-year period. *American journal of epidemiology*. 165, 12, 1364-1371.
- 18. Katz, D. L., Doughty, K. and Ali, A. 2011. Cocoa and chocolate in human health and disease. *Antioxidants & redox signaling*. 15, 10, 2779-2811.
- 19. Melton, A. W. 1963. Implications of short-term memory for a general theory of memory.
- 20. McDermott, K. B. and Roediger, H. L. 2016.Memory (encoding, storage, retrieval). Noba textbook series: Psychology. Champaign, IL: DEF publishers.
- 21. Uzun, S., Kozumplik, O. and Folnegović-Šmalc, V. 2011. Alzheimer's dementia: current data review. *Collegium antropologicum.* 35, 4, 1333-1337.
- 22. Glizer, D. and MacDonald, P. A. 2016. Cognitive training in Parkinson's disease: A review of studies from 2000 to 2014. *Parkinson's Disease*, 2016. 1-19.
- 23. Choi, J. and Twamley, E. W. 2013. Cognitive rehabilitation therapies for Alzheimer's disease: a review of methods to improve treatment engagement and self-efficacy. *Neuropsychology review*. 23, 1, 48-62.
- 24. Spencer, J. P. 2008. Food for thought: the role of dietary flavonoids in enhancing human memory, learning and neuro-cognitive performance: Symposium on 'Diet and mental health'. *Proceedings of the Nutrition Society*. 67, 2, 238-252.
- 25. Sokolov, A. N., Pavlova, M. A., Klosterhalfen, S. and Enck, P. 2013. Chocolate and the brain: neurobiological impact of cocoa flavanols on cognition and behavior. *Neuroscience &Biobehavioral Reviews*. 37, 10, 2445-2453.
- 26. Vauzour, D., Vafeiadou, K., Rodriguez-Mateos, A., Rendeiro, C. and Spencer, J. P. 2008. The neuroprotective potential of flavonoids: a multiplicity of effects. *Genes & nutrition*. 3, 3, 115.
- 27. Socci, V., Tempesta, D., Desideri, G., De Gennaro, L. and Ferrara, M. 2017. Enhancing Human cognition with cocoa flavonoids. *Frontiers in nutrition*. 4, 19.
- 28. Francis S. T, Head K, Morris P. G, Macdonald I. A. 2006. The effect of flavanol-rich cocoa on the fMRI response to a cognitive task in healthy young people. *J. Cardiovasc Pharmacol.* 47, 2, S221-3.
- 29. Kuriyama, S., Hozawa, A., Ohmori, K., Shimazu, T., Matsui, T., Ebihara, S. and Tsuji, I. 2006. Green tea consumption and cognitive function: a cross-sectional study from the Tsurugaya Project. *The American journal of clinical nutrition*. 83, 2, 355-361.
- 30. Larsson, S. C., Virtamo, J. and Wolk, A. 2012. Chocolate consumption and risk of stroke. A prospective cohort of men and meta-analysis. *Neurology*. 79, 12, 1223-1229.
- 31. Mastroiacovo, D., Kwik-Uribe, C., Grassi, D., Necozione, S., Raffaele, A., Pistacchio, L. andFerri, C. 2014. Cocoa flavanol consumption improves cognitive function, blood pressure control, and metabolic profile in elderly subjects: the Cocoa, Cognition, and Aging (CoCoA) Study—a randomized controlled trial. *The American journal of clinical nutrition*. 101, 3, 538-548.
- 32. Desideri, G., Kwik-Uribe, C., Grassi, D., Necozione, S., Ghiadoni, L., Mastroiacovo, D. and Marini, C. 2012. Benefits in cognitive function, blood pressure, and insulin resistance through cocoa flavanol consumption in elderly subjects with mild cognitive impairment: the Cocoa, Cognition, and Aging (CoCoA) study. *Hypertension, Hypertensionaha*. 112.
- Rendeiro, C., Vauzour, D., Rattray, M., Waffo-Téguo, P., Mérillon, J. M., Butler, L. T. and Spencer, J. P. 2013. Dietary levels of pure flavonoids improve spatial memory performance and increase hippocampal brain-derived neurotrophic factor. *PloS one*. 8, 5, e63535.
- 34. Middleton, E., Kandaswami, C. and Theoharides, T. C. 2000. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. *Pharmacological reviews*. 52, 4, 673-751.
- 35. Yao, L. H., Jiang, Y. M., Shi, J., Tomas-Barberan, F. A., Datta, N., Singanusong, R. and Chen, S. S. 2004. Flavonoids in food and their health benefits. *Plant foods for human nutrition*. 59, 3, 113-122.
- 36. Patel, J. 2008. A Review of Potential Health Benefits of Flavonoids. *Hdl.handle.net*. Retrieved August 15, 2019, from https://hdl.handle.net/10133/1220.

- 37. De Caterina, R., Zampolli, A., Del Turco, S., Madonna, R. and Massaro, M. 2006. Nutritional mechanisms that influence cardiovascular disease. *The American journal of clinical nutrition*. 83, 2, 421S-426S.
- 38. Rein, D., Paglieroni, T. G., Wun, T., Pearson, D. A., Schmitz, H. H., Gosselin, R. and Keen, C. L. 2000. Cocoa inhibits platelet activation and function. *The American journal of clinical nutrition*. 72, 1, 30-35.
- 39. Buijsse, B., Feskens, E. J., Kok, F. J. and Kromhout, D. 2006. Cocoa intake, blood pressure, and cardiovascular mortality: the Zutphen Elderly Study. *Archives of internal medicine*. 166, 4, 411-417.
- 40. Prasain, J. K., Carlson, S. H. and Wyss, J. M. 2010. Flavonoids and age-related disease: risk, benefits and critical windows. *Maturitas*. 66, 2, 163-171.
- 41. Ceriello, A. and Motz, E. 2004. Is oxidative stress the pathogenic mechanism underlying insulin resistance, diabetes, and cardiovascular disease? The common soil hypothesis revisited. *Arteriosclerosis, thrombosis, and vascular biology.* 24, 5, 816-823.
- 42. Reitz, C., Brayne, C. and Mayeux, R. 2011. Epidemiology of Alzheimer disease. *Nature Reviews Neurology*. 7, 3, 137.
- 43. Gill, S. S., Gupta, N., Bell, C. M., Rochon, P. A., Austin, P. C. and Laupacis, A. 2013. The timing of drug funding announcements relative to elections: a case study involving dementia medications. *PloS one*. 8, 2, e56921.
- 44. Spencer, J. P. 2010. The impact of fruit flavonoids on memory and cognition. *British Journal of Nutrition*. 104, S3, S40-S47.
- 45. Nurk, E., Refsum, H., Drevon, C. A., Tell, G. S., Nygaard, H. A., Engedal, K. and Smith, A. D. 2009. Intake of flavonoid-rich wine, tea, and chocolate by elderly men and women is associated with better cognitive test performance. *The Journal of nutrition*. 139, 1, 120-127.
- 46. Spencer, J. P. 2009. Flavonoids and brain health: multiple effects underpinned by common mechanisms. *Genes & nutrition.* 4, 4, 243.
- 47. Hussain, A., Mkpojiogu, E. O. C., & Kamal, F. M. (2016). Mobile video streaming applications: A systematic review of test metrics in usability evaluation. *Journal of Telecommunication, Electronic and Computer Engineering*, 8(10), 35–39.
- 48. Cheah, Y. K., Azahadi, M., Phang, S. N., and Manaf, N. H. A. 2018. Association of suicidal ideation with demographic, lifestyle and health factors in malaysians. *East Asian Archives of Psychiatry*, 28(3), 85-94.
- 49. Lifintseva, T.P. The buddhist pill for satre's "Nausea": Phenomenological and Hindu-Buddhist treatments of intentionality (2012) NeuroQuantology, 10 (4), pp. 670-675.
- 50. Dugić, M., Raković, D., Jeknić-Dugić, J., Arsenijević, M. The ghostly quantum worlds (2012) NeuroQuantology, 10 (4), pp. 619-628.
- 51. Arul Jothy, K., Sivakumar, K., & Delsey, M.J. (2018). Distributed System Framework for Mobile Cloud Computing. Bonfring International Journal of Research in Communication Engineering, 8(1), 5-9.
- 52. Kabeer, V., & Zainul Abid, T.P. (2013). Automated Face Recognition using Artificial Light Receptor Model and SVM Classifier. The SIJ Transactions on Computer Science Engineering & its Applications, 1(3), 36-41.