

Available online at www.sciencerepository.org

Science Repository



Review Article

The Role of Buffers in Establishing a Balance of Homeostasis and Maintaining Health

Jawad Alzeer*

Halalopathy, Swiss Scientific Society for Developing Countries, Zurich, Switzerland

ARTICLEINFO

Article history:

Received: 17 January, 2023 Accepted: 31 January, 2023 Published: 9 February, 2023

Keywords:
Entropy
potential energy
buffer
homeostasis
Le Chatelier principle
lifestyle
halalopathy

ABSTRACT

Homeostasis is the body's ability to self-regulate biological processes. There are several buffer systems in the body that operate cooperatively to maintain health. A buffer system consists of two components, one that acts on its counterpart. In acid-base homeostasis, almost all physiological processes in the body occur as a result of a buffer that allows a solution to tolerate pH changes. Buffers can be used beyond the concept of hydrogen ion donors or acceptors. A body consists of numerous components and their counterparts, such as excitatory and inhibitory neurotransmitters, entropy and potential energy, and anabolic and catabolic metabolic processes. As for values, they can be material and non-material; behaviours can be permitted or prohibited. Buffers play an important role in maintaining balance, but their capacity needs to be improved in order to handle stress more effectively. It is appropriate to evaluate buffering systems by analogy to acid-base buffers, and the results can be interpreted in terms of maintaining balance. A well-coordinated and compatible system helps maintain a balance between matter and its counterpart, enabling the immune system to function effectively and maintain homeostasis.

© 2023 Jawad Alzeer. Hosting by Science Repository.

Introduction

By default, human is exposed to many variables on a daily basis, and these variables can be mild, moderate, or severe. However, the human body is designed to cope with those variables and eventually deal with them either in form of metabolism, or immune response [1]. The efficiency of response is correlated with the capacity of homeostasis in the body [2]. Homeostasis is the process by which an organism or system maintains a stable, constant internal environment despite changing external conditions [3]. It is the way the body maintains a balance within its internal environment [4]. For example, the human body has many systems that work together to maintain homeostasis, such as the nervous system, the endocrine system, and the immune system [5]. These systems regulate various physiological processes such as body temperature, blood pressure, and levels of various chemicals in the body [6]. When homeostasis is disturbed, it can lead to various health problems or disorders.

For example, if the body's temperature regulation system is not working properly, it can lead to fever or hypothermia [7]. If the body's blood sugar

regulation system is not working properly, it can lead to diseases such as diabetes [8]. Buffers in general act to regulate imbalances and maintain homeostasis [9]. The buffer capacity is highly influenced by diet, age, stress, genetic makeup, and lifestyle [10, 11]. The term buffer was introduced to describe the ability of a solution to tolerate pH changes when exposed to strong acids or bases, allowing almost all physiological processes in the body to occur under acid-base homeostasis. Buffer solutions can resist pH changes as they contain a mixture of a weak acid and its conjugate base (antacid) and are able to neutralize H⁺ or OH⁻ ions that originate from a strong acid or base, respectively [12]. Buffer capacity is a measure of the ability of a buffer solution to resist changes in pH when small amounts of an acid or a base are added to it. It is a measure of the amount of acid or base that a buffer can neutralize before the pH of the solution begins to change significantly [13].

There are many different types of buffers that can be used, depending on the pH range that needs to be maintained and the specific chemical and biological requirements of the system. Some common biological buffer systems include the phosphate buffer, the bicarbonate buffer, and the amino acid buffer [14]. Buffer systems can be generalized for all aspects

^{*}Correspondence to: Jawad Alzeer, Halalopathy, Swiss Scientific Society for Developing Countries, Zurich, Switzerland; E-mail: jawad.alzeer@uzh.ch

of life. From a general perspective, the buffer system is primarily composed of matter and its counterpart, such as acid and antacid (base) [15]. The human body is composed of many facets that can exist together with its counterpart in a form of a buffer. Therefore, the components of buffers may go beyond the form of H^+ donors or acceptors to include, for example, neurotransmitters, metabolic reactions, and energy. In this context, we would like to explore the importance of these facets and their likely presence in the form of buffers, as well as the role of these buffer systems in maintaining homeostasis in the body and their impact on mental and physical health [16].

Homeostasis

The human body is designed to self-regulate biological processes and maintain internal stability [17]. A healthy body can better maintain its balance when it is in a state of homeostasis. The cells and organs of the body function properly when homeostasis maintains ideal body

temperature, pressure, pH, sugar levels, reaction rates, and many other vital biological processes [18]. As part of homeostasis, several buffer systems operate cooperatively in the body to maintain health (Figure 1). A buffer system is essentially composed of two components, the main component, and its counterpart component, each of which must be present at an appropriate balance and threshold to ensure more effective buffering [19]. In the body's aqueous solution, certain chemicals can behave in two ways: as hydrogen ion donors or acceptors. Similarly, there are two types of neurotransmitters: excitatory and inhibitory, two sources of energy: potential energy and entropy, and two main metabolic processes: anabolic and catabolic [20]. At the personal level, values can take two common forms: material and non-material; behaviour can take two modes: permitted and prohibited. It is appropriate to evaluate those potential buffering systems by analogy to acid-base buffers, and the results are interpreted in terms of maintaining balance and health [21, 22].

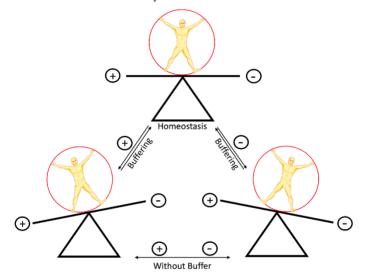


Figure 1: Homeostasis under buffering condition.

Acid-Base Buffer

Each protein in the cell belongs to a specific three-dimensional shape which is maintained by attractive forces that are located inside each protein [23]. In order for proteins to function optimally, cells secrete acids and bases to maintain the correct pH level [24]. Deviations in pH in either direction can result in serious health complications [25]. Using buffer solutions is a good way to maintain the pH at the optimal working level [26]. Buffer solutions are aqueous solutions consisting mainly of weak acids mixed with their conjugate bases or vice versa. Buffer solutions are designed to maintain a constant pH by absorbing small amounts of strong acids or bases. The amount of strong acids and bases are correlated with the buffer capacity, i.e. the higher the buffer capacity, the higher the tolerance threshold. The buffer capacity is controlled by the concentration of acid and its conjugate base in the solution.

In nature, buffers are essential for living cells, as a result, many living systems use buffers to regulate pH and maintain homeostasis. Phosphate, protein, and bicarbonate buffer systems are the most important buffer system in the body, with the bicarbonate buffer accounting for two-thirds

of the total buffer capacity. Buffers are most effective at resisting changes in pH within a narrow pH range around the pKa of the weak acid. The pKa is the pH at which the concentration of the weak acid and its conjugate base are equal. Bicarbonate buffers in the blood have a pH of 7.40 primarily composed of carbonic acid and its conjugate base, bicarbonate [27]. An excess of acids in the blood is called acidosis, while an excess of bases is called alkalosis. Any deviation in blood pH can affect organ function [12]. Symptoms of acidosis include lethargy, mental confusion, and impaired immune functioning due to decreased haemoglobin's affinity for oxygen [28]. Blood vessels narrow in alkalosis, reducing blood flow to the brain cells, and causing confusion, seizures, and unconsciousness [29].

Le Chatelier's Principle

In 1884, the French chemist and engineer Henry-Louis Le Chatelier introduced one of the central concepts of chemical equilibria, and later became known as Le Chatelier's principle [30]. It describes the effects on a system when it is temporarily brought out of equilibrium. According to Le Chatelier's principle, the location of the equilibrium, in the context

of chemical reaction, shifts either to the right or left depending on the change in concentration of either reactant or product. When an additional reactant is added to a system or when a product is removed from the system, equilibrium is shifted to the product. Similarly, equilibrium is shifted to reactant when the concentration of product is increased or the concentration of reactant is decreased. Therefore, the system always shifts its equilibrium in one of the two directions to counteract the change and restore balance [31].

Le Chatelier's principle was proposed to explain the effects of various factors on a system in equilibrium. According to this principle, an approach to regulate the viral load and potentially cure COVID-19 has been proposed [32]. This principle can also be applied to buffer solutions. When a base or an acid is added to a buffer solution, the equilibrium shifts in such a way that the effect of the added acid or base is minimized and the pH value is restored. Acid-base imbalance occurs when the pH of the blood is outside the normal range (7.35 to 7.45) due to significant impairment. As a result, the concentration of carbon dioxide in the blood changes, leading to a shift in the acid-base reaction and maintaining equilibrium in accordance with Le Chatelier's principle [33].

Neurotransmitter Buffer

Buffers in general act to regulate imbalances and maintain homeostasis [34]. The brain produces neurotransmitters in two forms, excitatory and inhibitory neurotransmitters. It is significant to maintain a balance between a load of excitatory and inhibitory neurotransmitters [35]. Distracting information can act as a source of either hyper-excitatory or hyper-inhibitory neurotransmitters. If the excitatory neurotransmitter predominates and lasts for a longer period of time, the neurotransmitter-based buffer system will be disrupted and anxiety will prevail.

If, on the other hand, inhibitory neurotransmitters dominate, depression prevails. Supportive information can serve as a source of balanced excitatory and inhibitory neurotransmitters that act as endogenous energy buffers [36]. The accumulation of balanced excitatory and inhibitory neurotransmitters leads to a more powerful buffer with high capacity. An effective neurotransmitter buffer with high capacity is necessary to maintain the appropriate level of harmony, regulate imbalances and maintain mental homeostasis [37]. The high potential energy is directly proportional to the high buffer capacity of the neurotransmitters. As a result, the immune system will dominate the fight mode, thus facilitating the prevention and control of disease [38].

Metabolic Buffer

Metabolism involves biochemical reactions to either produce vital molecules or release energy; the main metabolic processes are anabolic and catabolic metabolism [39]. The anabolic process plays an important role in generating vital molecules with high potential, while the catabolic process (anti-anabolic) serves as a source of internal energy [40]. To slow the aging process and maintain health, it is important to enrich the anabolic process and slow the catabolic process [41]. A balance in form of a buffer is needed to maintain between both processes. In youth, the anabolic process is dominant whereas in old age catabolic process is predominant. Both processes are interdependent, and a buffering

relationship needs to be maintained. Catabolic processes require macromolecules to generate internal energy, while anabolic processes require internal energy to build macromolecules. During old age, the anabolic process starts to slowdown mainly due to the accumulation of entropy, whereas the catabolic process remains effective as it is a spontaneous process. During this time, favourable circumstances should be created to ensure that the catabolic process and anabolic process remain actively balanced [42, 43].

Energy Buffer

Energy is the ability to perform work. Internal energy is primarily composed of potential energy and entropy, where potential energy is used to perform productive work, while entropy is used to release heat, which in turn is used to maintain body temperature [44]. Catabolic processes generate potential energy in the form of ATPs and entropy in the form of heat. ATPs are used for the anabolic process to build macromolecules that are rich in potential energy. Internal energy is stored in the structure of macromolecules in the form of constitution, configuration, and conformation. Macromolecules such as proteins or DNA are essential for life, and the stored potential energy is used to generate functions. Both forms of energy are important to keep the body active, productive, and vital [45]. These two forms of energy are inversely proportional, i.e. when entropy decreases, potential energy increases and vice versa [46]. Entropy needs to be slowed down as it is mostly spontaneously generated, while potential energy needs to be enriched as it is mostly non-spontaneously generated. A buffering relationship between the two forms is essential to keep life active. To maintain the balance between the two forms of energy, favourable circumstances are required that can enrich the potential and slow down the accumulation of entropy.

Value Buffer

By default, humans are driven by vital forces, one kind of which is fundamental and must be satisfied, while the other is essential and must be organized [47]. The fundamental vital forces are represented by organic needs that must be satisfied, while the essential vital forces are instincts that must be organized. Instincts can be divided into many categories, but primarily into survival and kind instincts. By default, we avoid everything that could endanger our lives and embrace everything that enriches our existence and supports humankind. For this purpose, however, it is necessary to build values. It is possible to divide values into two categories: material and non-material [48]. The material values can be felt physically and their usage can give pleasure, while other values are non-material, which can be recognized through the perception of confidence, certainty, and tranquility and their usage can give happiness. Most people enrich themselves with material values and only rarely with non-material values and therefore tend to assume that their value is equal to the value of what they possess.

Therefore, they spend most of their time working, earning money, and purchasing luxury goods. As soon as what they own is lost or used up, e.g., business collapses or job loss, their value drops to zero. Others try to balance material and non-material values by enriching their human, moral and spiritual values together with material values [49]. In general, people with balanced values are able to create a buffering relationship

between material and non-material things, hence people who choose this way of life are often happier, successful, productive, and confident. Therefore, a buffering relationship between material and non-material values is important to cope with the challenges and enable us to achieve our goal.

Lifestyle Buffer

Human is exposed to many variables on a daily basis, and these variables can be mild, moderate, or severe. The term lifestyle refers to the way a person lives their life by personalizing their daily habits, routines, and activities. It encompasses a wide range of factors that can influence an individual's health and well-being, including their diet, exercise, sleep habits, stress levels, and social interactions. Thus, a lifestyle is a set of thoughts that people choose to embrace, either because it solves a problem, especially a health problem, or because it is consistent with their fundamental beliefs [50]. There are many different factors that can influence a person's lifestyle, including age, culture, personal preferences, and environmental factors. There are a number of people who are sensitive to chemicals such as gluten, glucose, or lactose and therefore embrace a gluten-free, glucose-free, or lactose-free lifestyle that is appropriate to their chemical sensitivity and suitable for their health.

Other people are sensitive to animal ingredients and therefore adopt a vegetarian or vegan lifestyle. Many people expand their lifestyle capacities by choosing a lifestyle that derives from their fundamental beliefs and shapes their relationship with themselves, with others, and with their Creator [51]. For better harmonization, the development of a compatible system is essential. The enhancement of compatibility can be achieved by enriching the concept-behaviour relationship, maximizing cause-effect information, thereby increasing potential energy and reducing entropy. Lifestyle generally serves as a guide that can enrich our concepts and organize our behaviour when interacting with objects. The buffering capacity of the lifestyle varies and can be small or large depending on the balancing activities between permitted and not permitted actions. A high-capacity buffer manifests itself in the form of knowledge coupled with experience, and wisdom in solving problems, overcoming challenges, and coping with mental and physical stress. A higher buffering capacity more effectively coordinates the internal system and regulates internal imbalances for more effective homeostasis.

Discussion

The feelings and sensations are integral to our existence and have the capacity to influence our behaviour and reactions. The information we receive from our environment can affect our mental health and ultimately our physical integrity. For this purpose, the brain, acting as a central unit, controls all body activities and strives to maintain homeostasis in all aspects. Therefore, variables such as the concentration of chemicals, the rate of biochemical reactions, body temperature, and pressure must be kept in balance and harmony. All biochemical activities require energy. To monitor and maintain homeostasis, energy sources must be specified and provided from various sources and in different forms. Internal energy exists primarily in two forms, potential energy, and entropy. During catabolism, highly potential macromolecules are broken down, and their energy is converted into micro-molecules. Energy differences

between macromolecules and micro-molecules are converted into ATP and heat.

Thus, ATP molecules act as stored potential energy that is later used for anabolic processes, and heat is released in response to increasing entropy and used to maintain body temperature. A balance in the form of a buffer between the energy forms and thus between anabolic and catabolic processes must be established. Food generally serves as a source of chemical potential energy, but balanced mass control offers the opportunity to emphasize quality over quantity. A biodegradable, diversified diet compatible with lifestyle is recommended to control the catabolic process. The anabolic process can be enriched by activating growth hormones, which can be achieved by sufficient sleep, suitable sport, and intermittent fasting. Neurotransmitters can serve as a source of action potential energy that plays a role in speeding up or slowing down biochemical reactions. Information we receive can be distractive or supportive. Distractive information is any type of information that is designed to divert attention away from a particular topic or issue. It can be used to distract people from important or relevant information, or to deflect criticism or scrutiny. Distractive information can actually be a source of either excitatory or inhibitory neurotransmitters. Supportive information, on the other hand, can provide both neurotransmitters and thus serve as a source of balance between the two types of neurotransmitters, thereby enriching the neurotransmitters' buffering capacity.

Supporting information can provide a preview of what to expect, and thus we are prepared for a positive or negative outcome. Possession of material values is a driving force to achieve education, build a business, and civilized society. During the process of achieving the goal, problems can arise that lead to the collapse of education and/or business, and eventually to the complete loss of material value. When life is determined only by material values, the breakdown leads to losses, psychological problems, and eventually physical illnesses. Therefore, a buffering relationship between the material and non-material values is essential to overcome challenges and obstacles and eventually cope with collapse. Non-material values can be enriched by human, moral, and spiritual values, creating a balance with material values that is necessary to resist collapse and maintain the body's homeostasis. Lifestyles are meant to guide us on what is appropriate for us to do and what is not. Prohibited lifestyle activities are usually introduced to protect our health from harmful or sensitive substances and to maintain a balance with nonprohibited activities. The implementation of the lifestyle usually leads us to feel comfortable and achieve satisfaction in daily life. The capacity of the lifestyle buffer varies and can be small or large depending on the balancing activities between allowed and disallowed activities.

The role of a buffer in the body can be determined by comparing two aqueous solutions with the same pH. As an example, blood has a pH of 7.4. There are two ways to achieve a pH of 7.4 chemically: either dilute a weak base like sodium bicarbonate or mix a weak base with its conjugate acid like sodium bicarbonate and carbonic acid. In a solution consisting solely of bicarbonate, a strong acid or base will drastically alter the pH. A strong acid will lower the pH to 1, and a strong base will raise it to 14. However, an acid-base buffer solution can tolerate small addition of strong acid or base while maintaining a pH of about 7.4. As analogy, each component has the potential to exist with its counterpart,

thus buffering one another. If one component is present alone or in large quantities, the body will not be able to maintain balance, disrupting the body's homeostasis. If the component with its counterpart is present as a buffer and in the right proportion, the body will be able to maintain the balance and thus enhance homeostasis. Despite the importance of buffers in keeping balance, buffer capacity must be improved in order to handle stress more effectively.

Halalopathy has been introduced as a new concept in medicine to cope with entropy and enrich potentials [52, 53]. The concept provides prevention of diseases by strengthening the immune system's fight mode and curing diseases by creating a compatible system. The fight mode can be activated by reducing fear and grief, enriching tranquility and potential, while the cure for disease can be achieved by combining medicine and lifestyle, activating compatibility and thereby enriching the buffering capacity of lifestyle. The creation of a well-organized system between lifestyle and therapeutic drugs reduces entropic overload and maintains a balance between potential energy and entropy, which is useful for maintaining homeostasis and activating the immune system. Entropy occurs spontaneously, but potential energy does not. Therefore, it is necessary to promote conditions that result in the accumulation of potential energy and reduction of entropy so that the immune system works synergistically with the prescribed drugs to improve healing and promote full recovery. According to halalopathy, the concept of entropy is described by spontaneous processes or involuntarily acquired energy and enriched by the catabolic process as well as the pleasure and pain associated with material values. Potential energy, on the other hand, is a non-spontaneous aspect of voluntarily acquired energy that can be enriched by the activation of anabolic processes and by happiness resulting from non-material values [40]. Maintaining homeostasis ensures the body's health and balance through a buffering relationship between lifestyle, values, and energy.

Conclusion

Humans and other organisms function optimally when the body is in homeostasis, a state that ensures a balance between a wide range of processes and functions. Buffers act to maintain homeostasis by regulating imbalances. Diet, age, stress, genetic makeup, and lifestyle greatly influence buffer capacity. During biochemical reactions, energy is required for all activities. Potential energy and entropy are the primary forms of internal energy that is needed to maintain homeostasis. Balance in form of a buffer must be established between energy forms and between anabolic and catabolic processes. Providing supportive information can produce both excitatory and inhibitory neurotransmitters, thus enhancing the ability of neurotransmitters to buffer each other. Non-material values can be enhanced by enriching human, moral, and spiritual values, creating a balance with material values that is necessary to overcome challenges and eventually cope with collapse. Healthcare systems that are coordinated and regulated can ensure that behaviour and concept are well integrated. A therapeutic drug compatible with lifestyle preferences increases lifestyle buffering capacity, which increases immunity and increases overall potential.

Acknowledgment

We would like to thank Prof. Loay Awad, Prof. Khaled Abou Hadeed, and Reem Alzeer for their useful discussion and support.

Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest

None.

REFERENCES

- Chouhan DS (2016) Stress and Its Major Effects on Human Health. *International Journal of Multidisciplinary Allied Research Review and Practices* 3: 380-384.
- Chovatiya R, Medzhitov R (2014) Stress, inflammation, and defense of homeostasis. Mol Cell 54: 281-288. [Crossref]
- Billman GE (2020) Homeostasis: The Underappreciated and Far Too Often Ignored Central Organizing Principle of Physiology. Front Physiol 11: 200. [Crossref]
- Asarian L, Gloy V, Geary N (2012) Homeostasis. In V. S. Ramachandran (Ed.), Encyclopedia of human behaviour, 2nd edition, San Diego, CA: Academic Press, 324-333.
- Jin R, Luo L, Zheng J (2022) The Trinity of Skin: Skin Homeostasis as a Neuro-Endocrine-Immune Organ. Life (Basel) 12: 725. [Crossref]
- Savioli G, Zanza C, Longhitano Y, Nardone A, Varesi A et al. (2022)
 Heat-Related Illness in Emergency and Critical Care:
 Recommendations for Recognition and Management with Medico Legal Considerations. *Biomedicines* 10: 2542. [Crossref]
- Osilla EV, Marsidi JL, Sharma S (2022) Physiology, Temperature Regulation. StatPearls Publishing, [Crossref]
- Röder PV, Wu B, Liu Y, Han W (2016) Pancreatic regulation of glucose homeostasis. Exp Mol Med 48: e219. [Crossref]
- Hamm LL, Nakhoul N, Hering Smith KS (2015) Acid-Base Homeostasis. Clin J Am Soc Nephrol 10: 2232-2242. [Crossref]
- Vormann J, Goedecke T (2006) Acid-Base Homeostasis: Latent Acidosis as a Cause of Chronic Diseases. Schweiz Zschr GanzheitsMedizin 18: 255-266.
- 11. Hultsch DF, Hertzog C, Small BJ, Dixon RA (1999) Use it or lose it: engaged lifestyle as a buffer of cognitive decline in aging? *Psychol Aging* 14: 245-263. [Crossref]
- Gehlbach BK, Schmidt GA (2004) Bench-to-bedside review: treating acid-base abnormalities in the intensive care unit - the role of buffers. Crit Care 8: 259-265. [Crossref]
- de Oliveira AF (2020) Buffering Function: A General Approach for Buffer Behavior. The Journal of Engineering and Exact Sciences 6: 0387-0396.
- Zhou H, Singh H, Parsons ZD, Lewis SM, Bhattacharya S et al. (2011)
 The biological buffer bicarbonate/CO₂ potentiates H₂O₂-mediated inactivation of protein tyrosine phosphatases. *J Am Chem Soc* 133: 15803-15805. [Crossref]

- Ribeiro MDLC, Silva AS, Bailey KM, Kumar NB, Sellers TA et al. (2012) Buffer Therapy for Cancer. J Nutr Food Sci 2: 6. [Crossref]
- Livshits G, Roset A, Yakovenko K, Trofimov S, Kobyliansky E (2002) Genetics of human body size and shape: body proportions and indices. Ann Hum Biol 29: 271-289. [Crossref]
- 17. Fotopoulou A, Tsakiris M (2017) Mentalizing homeostasis: The social origins of interoceptive inference. *Neuropsychoanalysis* 19: 3-28.
- Modell H, Cliff W, Michael J, McFarland J, Wenderoth MP et al. (2015) A physiologist's view of homeostasis. *Adv Physiol Educ* 39: 259-266. [Crossref]
- Nakada T (2010) Conversion of brain cytosol profile from fetal to adult type during the perinatal period: taurine-NAA exchange. *Proc Jpn Acad Ser B Phys Biol Sci* 86: 630-642. [Crossref]
- Pang G, Xie J, Chen O, Hu Z (2014) Energy Intake, Metabolic Homeostasis, and Human Health. Food science and human wellness 3: 89-103.
- Dambrun M (2017) Self-centeredness and selflessness: happiness correlates and mediating psychological processes. *PeerJ* 5: e3306. [Crossref]
- Piko BF, Brassai L (2016) A reason to eat healthy: The role of meaning in life in maintaining homeostasis in modern society. *Health Psychol Open* 3: 2055102916634360. [Crossref]
- Lammert H, Wolynes PG, Onuchic JN (2012) The role of atomic level steric effects and attractive forces in protein folding. *Proteins* 80: 362-373. [Crossref]
- Molinari G, Molinari L, Nervo E (2020) Environmental and Endogenous Acids Can Trigger Allergic-Type Airway Reactions. Int J Environ Res Public Health 17: 4688. [Crossref]
- Kuo SH, Shen CJ, Shen CF, Cheng CM (2020) Role of pH Value in Clinically Relevant Diagnosis. *Diagnostics (Basel)* 10: 107. [Crossref]
- Brudar S, Hribar Lee B (2021) Effect of Buffer on Protein Stability in Aqueous Solutions: A Simple Protein Aggregation Model. J Phys Chem B 125: 2504-2512. [Crossref]
- Quade BN, Parker MD, Occhipinti R (2021) The therapeutic importance of acid-base balance. *Biochem Pharmacol* 183: 114278. [Crossref]
- Diez Fernandez C, Rüfenacht V, Santra S, Lund AM, Santer R et al. (2016) Defective hepatic bicarbonate production due to carbonic anhydrase VA deficiency leads to early-onset life-threatening metabolic crisis. *Genet Med* 18: 991-1000. [Crossref]
- Tinawi M (2021) Pathophysiology, Evaluation, and Management of Metabolic Alkalosis. Cureus 13: e12841. [Crossref]
- Henry LC (1884). On a general statement of the laws of chemical equilibrium. Comptes Rendus de l'Académie des Sciences 99: 786-789.
- Middelburg JJ, Soetaert K, Hagens M (2020) Ocean Alkalinity, Buffering and Biogeochemical Processes. Rev Geophys 58: e2019RG000681. [Crossref]
- 32. Alzeer J, Al Razem F (2021) Hypotheses: implementation of Le Chatelier's principle as a potential integrative method to prevent and or cure coronavirus. *J Public Health Emerg* 5: 1-7.
- Arazawa DT, Kimmel JD, Federspiel WJ (2015) Kinetics of CO₂ exchange with carbonic anhydrase immobilized on fiber membranes in artificial lungs. *J Mater Sci Mater Med* 26: 193. [Crossref]

- Pendyam S, Mohan A, Kalivas PW, Nair SS (2012) Role of perisynaptic parameters in neurotransmitter homeostasiscomputational study of a general synapse. Synapse 66: 608-621.
- Tatti R, Haley MS, Swanson OK, Tselha T, Maffei A (2017) Neurophysiology and Regulation of the Balance Between Excitation and Inhibition in Neocortical Circuits. *Biol Psychiatry* 81: 821-831.
 [Crossref]
- Alzeer J (2022) Halalopathy: Anxiety and depression from logic and energetic perspectives. Am J Biomed Sci & Res 16: 378-384.
- Scimemi A, Beato M (2009) Determining the neurotransmitter concentration profile at active synapses. *Mol Neurobiol* 40: 289-306.
 [Crossref]
- Alzeer J (2022) Halalopathy: Stimulation of the Immune System Through Enrichment of Potential Energy. Int J Regent Med 5: 1-5.
- Valenti G, Schwartz RS (2008) Anabolic decline in the aging male: a situation of unbalanced syncrinology. Aging Male 11: 153-156.
 [Crossref]
- Alzeer J (2022) Directionality of chemical reaction and spontaneity of biological process in the context of entropy. Int J Regent Med 5: 1-7.
- Alzeer J (2022) Halalopathy: Role of Entropy in the Aging Process. Am J Biomed Sci & Res 16: 147-154.
- 42. Mueller MB, Tuan RS (2011) Anabolic/Catabolic balance in pathogenesis of osteoarthritis: identifying molecular targets. *PM R* 3: S3-S11. [Crossref]
- Alzeer J (2022) Halalopathy: Revival of Miraculous Cure and Creation of Favourable Circumstances for Cancer Therapy. *Medicon Medical* Sciences 2: 21-28.
- Alzeer J (2022) Halalopathy: Improving Potential Energy and Minimising Entropy offer an Integrative approach for more Effective Treatment. Medicon Medical Sciences 2: 21-24.
- Hill JO, Wyatt HR, Peters JC (2013) The Importance of Energy Balance. Eur Endocrinol 9: 111-115. [Crossref]
- Alzeer J (2020) Entropy and potential energy as a key role of halalopathy in disease prevention and cure. Longhua Chin Med 3: 20.
- 47. Masi M (2022) Vitalism and cognition in a conscious universe.

 *Commun Integr Biol 15: 121-136. [Crossref]
- Sténs A, Bjärstig T, Nordström EM, Sandstrom C, Fries C et al. (2016)
 In the eye of the stakeholder: The challenges of governing social forest values. Ambio 45: 87-99. [Crossref]
- Zsolnai, L (2015) Materialistic versus non-materialistic valueorientation in management. In: K.J. Ims and L.J.T. Pedersen (eds) Business and the Greater Good, Cheltenham, UK: Edward Elgar Publishing Limited 107-116.
- Alzeer J, Hadeed KA (2021) Halal Certification of Food, Nutraceuticals, and Pharmaceuticals in the Arab World. In: Laher I. (eds) Handbook of Healthcare in the Arab World. Cham: Springer, 765-787
- Alzeer J (2021) Permissible Medicine and Rationalization of Halal Pharma. Halalpshere 1: 43-52.
- Alzeer J (2018) Halalopathic: A New concept in Medicine. J Mol Genet Med 12: 353.
- 53. Alzeer J (2019) Halalopathy: A science of trust in medicine. *J Integr Med* 17: 150-154. [Crossref]