ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research

Vol. 16, Issue, 09, pp.29763-29768, September, 2024
DOI: https://doi.org/10.24941/ijcr.47719.09.2024

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

REVIEW ARTICLE

THEORETICAL BASIS OF DIABETESTREATMENTIN THE FRAMEWORK OFTHE NEW CONCEPTION RELATING TO THE CLOSED 9-STEPPED CYCLE OF PROTON CONDUCTANCE

Ambaga, M., Kulan, TS.,Tumen-Ulzii, A., Buyantushig. T.

New Medicine Medical University, Ulanbator, Mongolia

ARTICLE INFO

Article History:
Received 20th June, 2024
Received in revised form
19th July, 2024
Accepted 19th August, 2024
Published online 30th September, 2024

Key words:
Closed 9-stepped cycle, return to original state.

***Corresponding author:**
Mallappa Shalavadi

ABSTRACT

Closed 9-stepped cycle,proposedby M.Ambaga means that after completing all 9 stages, the system returns to its original state. The movement of protons is cyclic, with no net loss or gain of protons in the overall system, just a continuous movement within the defined cycle. The cycle being closed ensures that the process is efficient and self-sustaining, as it doesn't require new inputs from outside once the cycle is running. In biological systems, such cycles are important for energy conservation and regulation of processes like ATP synthesis. During Diabetes have beendisturbed the above mentioned Normal thermodynamic processes, conducted in the Closed 9-stepped cycle of proton conductance as exergonic reactions are favorable, or spontaneous reactions, no needed new inputs from outside, self-sustaining, after completing all 9 stages, the system returns to its original state. It can be say that according to the Closed 9-stepped cycle of proton conductance, the molecular mechanism of diabetes have been characterized by pathological increase of glucose in the second compartmernt – extacellular -blood serum location (hyperglycemia) of Human body and pathological decrease of glucose in the first compartment of Human body , because of in this case have been occurred the decrease of entry of glucose to metabolic medium as "Donators of proton as glucose molecules (first stage of proton conductance) + membrane redox potentials in the three-state line system + O_2 (hemoglobin of the pulmonary capillary -8-th stage, hemoglobin of tissue-87 trillion cell-surrounded capillary-9-th stage) + ADP + Pi + (H^+ + nH + memb.space - proton gradient-4-th stage) = (ATP + heat energy-5-th stage) + H_2O (5-th stage) + (nH + matrix) + CO_2(second stage of proton conductance).

Citation: Ambaga, M., Kulan, TS.,Tumen-Ulzii, A., Buyantushig. T.. 2024. "Theoretical basis of Diabetestreatmentin the framework ofthe new conception relating to the Closed 9-stepped cycle of proton conductance*". International Journal of Current Research*, 16, (09), 29763-29768.

INTRODUCTION

It was interesting to explain the action mechanism of Mongolian Honey bee venom blood glucose reducing effect in accordance with a new variant of the metabolic equation proposed by us as "Donators of proton as glucose molecules (first stage of proton conductance) + membrane redox potentials in the three-state line system + O_2 (hemoglobin of the pulmonary capillary -8-th stage, hemoglobin of tissue-87 trillion cell-surrounded capillary-9-th stage) + ADP + Pi + (H^+ + nH + memb.space - proton gradient-4-th stage) = (ATP + heat energy-5-th stage) + H_2O (5-th stage) + (nH + matrix) + CO_2(second stage of proton conductance). During our previous study was established that Mongolian Honey bee venom (Apis melilifera) reduces Hyperglycemia and Hyperlipidemia in Alloxan induced Diabetic rabbits. In such way, the desturbances,happened during Alloxan induced Diabetes in the Eigth stage of proton conductance, where proton released from R-state hemoglobin enhances CO_2 release in the respiratory membranes of the lungs; the dramatic increase in the partial pressure of oxygen drives the binding of oxygen to deoxyhemoglobin; O_2 binding triggers the transition of T-state hemoglobin to R-state hemoglobin and the disturbance occurred in the Ningh stage, where binding of protons to T-state hemoglobin increases CO_2 uptake from respiring tissues, as R-state hemoglobin gives up its bound oxygen to respiring tissues and subsequently transitions to the T-state, it drives the release of oxygen from hemoglobin to the mitochondria of 87 trillion cells. Carbon dioxide and hydrogen ions combine with hemoglobin, which has released oxygen from hemoglobin, which diffuses out of red blood cells and plasma into tissues (the mitochondria) lead to Hyperglycemia and Hyperlipidemia. Diabetes is disease, happened in closed cycle of proton conductance, that is process cyclic, returning to its initial state after completing all steps, which is characteristic of many biological processes to ensure efficient and continuous operation. In such a cycle protons are moved in a stepwise manner through series of intermediate states.

The closed 9-stepped cycle of proton conductance by M. Ambaga refers to a theoretical model or mechanism that explains the conductance of protons through specific proteins or structures, such as those found in biological membranes. Proton conductance is crucial in processes like cellular respiration and photosynthesis, where protons are transported across membranes to create a proton gradient that drives ATP synthesis. In such a cycle, protons are moved in a stepwise manner through a series of intermediate states, often involving conformational changes in the protein that allow the proton to be transported from one side of the membrane to the other. The "9-stepped" aspect suggests that this process involves nine distinct steps or transitions, which might include various binding and release events, changes in the protein structure, and the transfer of protons between different sites. The term "closed cycle" implies that the process is cyclic, returning to its initial state after completing all steps, which is a characteristic of many biological processes to ensure efficient and continuous operation.

MATERIALS AND METHODS

Twenty two Chinchilla rabbits were divided into three groups: the control (n=6),the diabetic (n=8), and the bee venom treated (n=8) groups. The diabetic group was injected with a 5 % solution of Alloxan monohydrate at 100 mg/kg intravenously via the marginal vein behind the ear for 2 minutes to induce the diabetes . The bee venom treated group received a bee sting (a sting contains 0,2-0,5 ml of bee venom) on their hind paw every other day after the confirmation of diabetes (20).

RESULTS

During our experiments became clear that Hyperglycemia and Hyperlipidemia in Alloxan induced Diabetic Rabbits have been induced by pathological increase of glucose in the second compartmernt – blood serum location (hyperglycemia) and pathological decrease of glucose in the first compartment of Body (Tab 1, 2 and Figure 1, 2) because of decrease of entry of glucose to metabolic medium as “Donators of proton as glucose molecules (first stage of proton conductance) + membrane redox potentials in the three-state line system + O2 (hemoglobin of the pulmonary capillary -8-th stage, hemoglobin of tissue-87 trillion cell-surrounded capillary-9-th stage) + ADP + Pi + (H^+ + nH + memb.space - proton gradient-4-th stage) = (ATP + heat energy-5-th stage) + H_2O (5-th stage) + (nH + matrix) + CO_2(second stage of proton conductance).
The results of our investigation gives the possibility to say that During Diabetes have beenDisturbed the Normal thermodynamicprocesses, conducted in the Closed 9-stepped cycle of proton conductance as exergonic reactions are favorable, or spontaneous reactions, no needed new inputs from outside, self-sustaining, after completing all 9 stages, the system returns to its original state.

We should be pay attention to this that decrease of glucose in the second compartment (extracellular- serum) of body is accompanied by decrease of glucose in the first compartment (Metabolic equation medium).

Figure 1. Changes in blood glucose levels in the second compartment (extra cellular -serum) after bee venom treatment of diabetic rabbits.

Bee venom treatment (BVT) led to the following changes: compared to the diabetic group, the bee venom treated group’s blood glucose levels decreased by 14.9% -26.5%; blood cholesterol levels reduced by 12.5%- 19.1%; Low Density Lipoproteins (LDL) levels lowered by 11.2%-14.2%; and High Density Lipoproteins (HDL) levels increased by 2.5% - 26.25%. Conclusion: Bee venom lowers blood glucose levels and improves lipid profile in alloxan-induced diabetic rabbits and can be considered as a therapeutic agent for diabetes. Further studies should be carried out to determine the most appropriate bee venom dose for the best therapeutic effect. The action mechanism of Mongolian Honey bee venom blood glucose reducing effect should be clear in case of using the new variant of the metabolic equation, proposed by“Proton Donators as glucose (first stage of proton conductance- figure 4-1) + membrane redox potentials in the three-state line system + O_2 (hemoglobin of the pulmonary capillary -8-th stage-figure 4-8 , hemoglobin of tissue-87 trillion cell-surrounded capillary-9-th stage- figure 4-9) + ADP + Pi + (H^+ + nH + memb.space - proton gradient-4-th stage) = (ATP + heat energy-5-th stage-figure 4-5) + H_2O (5-th stage) + (nH + matrix) + CO_2(second stage of proton conductance).

The disturbance,happened in the First stage of proton conductance as one of reasons of Diabetes, oxygen channeling to the mitochondria of 87 trillion cells, oxygen has been assumed to diffuse across cell bodies; very low oxygen solubility in the cytosol, High-solubility ‘channels’ likely formed by the endoplasmic reticulum by hemoglobin-bearing cytochrome P450 molecules; accelerated oxygen diffusion via lipid droplets; lateral diffusion within mitochondrial membranes; release of hydrogen atoms, protons, and electrons from food molecules; Krebs cycle under the influence of the ninth stage as release of oxygen from hemoglobin may be decreased under effect of Mongolian Honey bee venom. In such way, also disturbance,happened in the second stage of proton conductance as where carbon dioxide, generated by the Krebs cycle in the mitochondria of 87 trillion cells,andthird stage, where conducted the formation of NADH, FADH, Coenzyme Q, and Cytochrome C oxidase, the fifth stage, where conducted the formation of ATP, heat energy, and metabolic watermay be one of reasons of antiabetes effectof Mongolian Honey bee venom. Beside, the disturbance,happened in the Eigth stage of proton conductance, where proton released from R-state hemoglobin enhances CO_2 release in the respiratory membranes of the lungs; the dramatic increase in the partial pressure of oxygen drives the binding of oxygen to deoxyhemoglobin; O_2 binding triggers the transition of T-state hemoglobin to R-state hemoglobin andthe disturbance,happened in the Ningh stage, where binding of protons to T-state hemoglobin increases CO_2 uptake from respiring tissues,as R-state hemoglobin gives up its bound oxygen to respiring tissues and subsequently transitions to the T-state, it drives the release of oxygen from hemoglobin to the mitochondria of 87 trillion cells. Carbon dioxide and hydrogen ions combine with hemoglobin, which has released oxygen, to promote the release of oxygen from hemoglobin. Oxygen is released from hemoglobin, which diffuses out of red blood cells and plasma into tissues (the mitochondria) may be decreased under effect of Mongolian Honey bee venom blood glucose reducing effect Closed 9-stepped cycle, proposed by M.Ambaga means that after completing all 9 stages, the system returns to its original state. The movement of protons is cyclic, with no net loss or gain of protons in the overall system, just a continuous movement within the defined cycle.

Measured biochemical parameters in the second compartment (extra cellular -serum)	Groups	Day 1
Glucose mmol/l	Control	5.52±0.18
	Diabetic	21.65±2.2
	BVT	15.92±1.53
Chlolesterol mmol/l	Control	3.20±0.15
	Diabetic	4.92±0.51
	BVT	4.75*±0.32
Tryglyceride mmol/l	Control	1.20±0.07
	Diabetic	2.59**±0.21
	BVT	2.24±0.15
LDL mmol/l	Control	2.09±0.08
	Diabetic	2.97*±0.32
	BVT	2.69±0.42
HDL mmol/l	Control	1.71±0.05
	Diabetic	1.66±0.07
	BVT	2.03±0.33

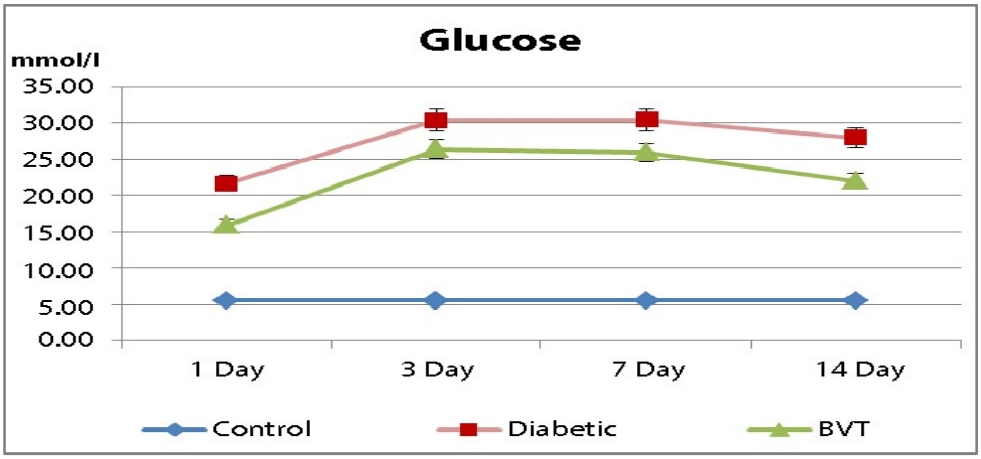


Figure 1. Changes in blood glucose levels in the second compartment (extra cellular -serum) after bee venom treatment of diabetic rabbits

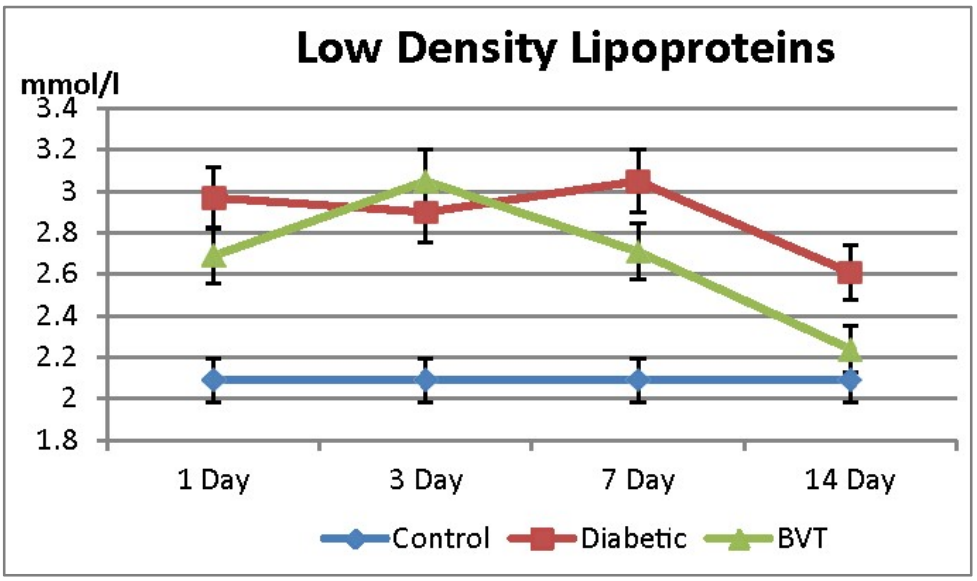


Figure 2. Changes in blood low density lipoproteins in the second compartment (extra cellular -serum after Bee venom treatment of diabetic rabbits

The cycle being closed ensures that the process is efficient and self-sustaining, as it doesn't require new inputs from outside once the cycle is running. In biological systems, such cycles are important for energy conservation and regulation of processes like ATP synthesis. During Diabetes have beendisturbed the above mentioned Normal thermodynamic processes, conducted in the Closed 9-stepped cycle of proton conductance as exergonic reactions are favorable, or spontaneous reactions, no needed new inputs from outside, self-sustaining, after completing all 9 stages, the system returns to its original state. It can be say that according to the Closed 9-stepped cycle of proton conductance, the molecular mechanism of diabetes have been characterized by pathological increase of glucose in the second compartmernt - extacellular -blood serum location (hyperglycemia) of Human body and pathological decrease of glucose in the first

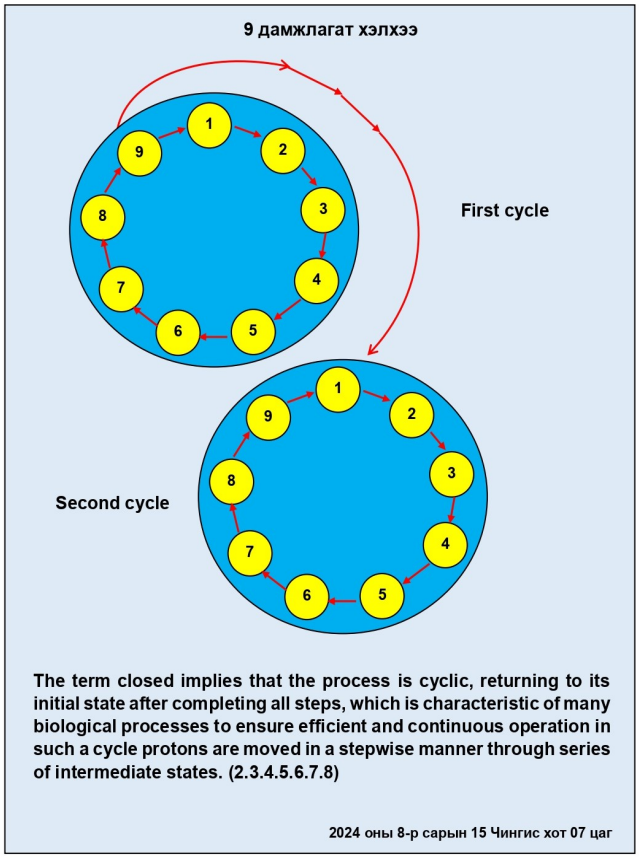
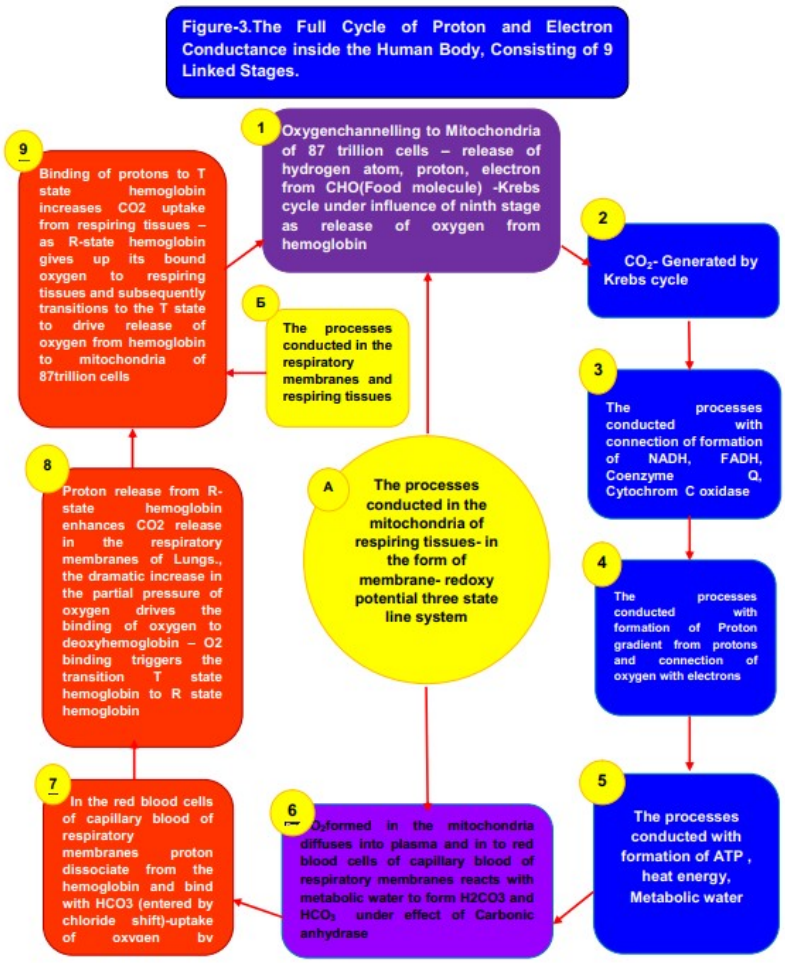


Figure 4. The closed cycle of proton conductance by M.Ambaga, that is process cyclic, returning to its initial state after completing all steps



compartment of Human body, because of in this case have been occurred the decrease of entry of glucose to metabolic medium as "Donators of proton as glucose molecules (first stage of proton conductance) + membrane redox potentials in the three-state line system + O_2 (hemoglobin of the pulmonary capillary -8-th stage, hemoglobin of tissue-87 trillion cell-surrounded capillary-9-th stage) + ADP + Pi + (H^+ + nH + memb.spe - proton gradient-4-th stage) = (ATP + heat energy-5-th stage) + H_2O (5-th stage) + (nH + matrix) + CO_2(second stage of proton conductance). It can be say that according to closed cycle of proton conductance proposed M.Ambaga (5) the molecular mechanism of diabetes have been characterized pathological increase of glucose in the second compartmernt – blood serum location (hyperglycemia) of Human body and pathological decrease of glucose in the first compartment of Human body (2,16,17) because of decrease of entry of glucose to metabolic medium as "Donators of proton as glucose molecules (first stage of proton conductance) + membrane redox potentials in the three-state line system + O2 (hemoglobin of the pulmonary capillary -8-th stage, hemoglobin of tissue-87 trillion cell-surrounded capillary-9-th stage) + ADP + Pi + (H^+ + nH + memb.space - proton gradient-4-th stage) = (ATP + heat energy-5-th stage) + H_2O (5-th stage) + (nH + matrix) + CO_2(second stage of proton conductance).

The disturbance,happened during Alloxan induced Diabetes in the First stage of proton conductance: oxygen channeling to the mitochondria of 87 trillion cells; oxygen channeling: oxygen has been assumed to diffuse across cell bodies; very low oxygen solubility in the cytosol, reported High-solubility 'channels' likely formed by the endoplasmic reticulum by hemoglobin-bearing cytochrome P450 molecules; accelerated oxygen diffusion via lipid droplets; lateral diffusion within mitochondrial membranes; mitochondria; release of hydrogen atoms, protons, and electrons from food molecules; Krebs cycle under the influence of the ninth stage as release of oxygen from hemoglobin may be decreased under effect of Mongolian Honey bee venom blood glucose reducing effect
In such way,the second stage of proton conductance wherecarbon dioxide, generated by the Krebs cycle in the mitochondria of 87 trillion cells,and third stage, where conducted the formation of NADH, FADH, Coenzyme Q, and Cytochrome C oxidase. The fifth stage, where conducted the formation of ATP, heat energy, and metabolic water., the sixth stage, where CO_2 and metabolic water formed in the mitochondria and diffused into plasma and into red blood cells, all these regulations pathologically disturbed because of Hyperglycemia and Hyperlipidemia in Alloxan induced Diabetic Rabbits have decreased under effect of Mongolian Honey bee venom blood glucose reducing effect. Beside, the desturbances,happened during Alloxan induced Diabetes in the Eigth stage of proton conductance, where proton released from R-state hemoglobin enhances CO_2 release in the respiratory membranes of the lungs; the dramatic increase in the partial pressure of oxygen drives the binding of oxygen to deoxyhemoglobin; O_2 binding triggers the transition of T-state hemoglobin to R-state hemoglobin and the disturbance occurred in theNingh stage, where binding of protons to T-state hemoglobin increases CO_2 uptake from respiring tissues, as R-state hemoglobin gives up its bound oxygen to respiring tissues and subsequently transitions to the T-state, it drives the release of oxygen from hemoglobin to the mitochondria of 87 trillion cells. Carbon dioxide and hydrogen ions combine with hemoglobin, which has released oxygen from hemoglobin, which diffuses out of red blood cells and plasma into tissues the mitochondria) lead to Hyperglycemia and Hyperlipidemia. Diabetes is disease disturbed the closed cycle of proton conductance, that is process cyclic, returning to its initial state after completing all steps, which is characteristic of many biological processes to ensure efficient and continuous operation. In such a cycle protons are moved in a stepwise manner through series of intermediate states (2,3,4,5,6,7,8).

REFERENCES

1.Ambaga M, Tumen-Ulzii A. 2016. Integrated NCM medicine with s-NCM new knowledge, lambert Academic Publishing.

2.Ambaga M, Tumen-Ulzii A. 2015. The life become dependent from the presence of electrons and protons, which were formed during events called big bang 15 billion years ago, electrons and protons sets the stage for formation of life in the universe

3. Ambaga M. 2016. The Full Cycle of Proton and Electron Conductance inside the Human Body, Consisting of 9 Linked Stages. *Acad. J. Sci. Res.,* 4(6): 127-131.

4.Ambaga M. 2016. A new suggestionabout existing of membrane -redoxy potential three state line system between donators and acceptors inside the living cells, *Asian Journal of Science and Technology,* Vol.07, Issue,07,pp.3157-3161.

5. Ambaga M. 2016. The buffering capacity of erythrocyte membrane surroundings in relation to free protons, formed in the Full Cycle of Proton and Electron Conductance inside the Human Body. *International Journal of Development Research,*Vol 06, Issue, 07, pp. 8458-8461.

6. Ambaga M. 2016. The Full Cycle of Proton and Electron Conductance inside the Human Body and triple Rlung, Mkhris, Badgan theory of Tibetian Traditional medicine, *International Journal of Current Research, Vol 8, Issue 08, p.36391-36393.*

7. Ambaga M. 2016. The possibility to drive the membrane - redox potential, a three state line system dependent-full 9 stepped cycle of proton conductance inside human body to favorable directionduring pathological situations.,*International Journal of Current Research,* Vol, Issue, 11, pp 42456-42459, November.

8. Ambaga M. 2017. The membrane-redox potentials three-state line system dependent -full 9 stepped cycle of proton conductance and the evolution based biological mechanism of oxygen utilization –ATP making bioenergy systems, *World Journal of Scientific Research and Review,* 2017.vol.5,№ 3,march,pp.8-13.

9.Ambaga M. 2017. The membrane-redox potentials three-state line system dependent -full 9 stepped cycle of proton conductance and the evolution based biological mechanism of organ formation, *World Journal of Scientific Research and Review,* vol.5,№ 3,march,pp.1-7.

10. Ambaga M. 2017. The membrane-redox potentials three-state line system dependent -full 9 stepped cycle of proton conductance as the universal metabolic formula and the development of all medical thinking during last 3000 years, *Asian Journal of Science and technology,* vol.08,Issue,03,pp.4485-4488, March,

11.Ambaga M. 2017. The full 9 stepped cycle of proton conductance and the two basic electron, proton dependent metabolic reaction system of obtaining of ATP, *Applied Science and innovative Research,* vol.1,No 1,pp 63-68 .

12.Ambaga M. 2017. The bioevolution link between the two basic electron, proton dependent metabolic reaction systems of obtaining of ATP, *International Journal of Current Research,* vol 9,issue 06,pp.52182-52185.
13.Ambaga M. 2017. The genome size and the two basic electron,proton dependent metabolic reaction systems of obtaining of ATP, *International Journal of Current Research,* vol 9,issue 06,pp.52771-52774.
14. Ambaga M, Tumen-Ulzii A,2017. The full 9 stepped cycle of proton conductanceand antispiral-like evolutionary back steps from second late evolution time equation to first early evolution time equation during some pathology, *International Journal of Current Research,* vol 9,issue 07,pp.54969-54972.
15.Ambaga M,Tumen-Ulzii A,2017. The full 9 stepped cycle of proton conductanceand the formation of three zones with various degree of disturbances of clockwise normal flow of electrons and protons during shortage of donators and acceptors- *Asian Journal of Science and technology,* vol.08,Issue,08,pp.5346-5349,
16.Ambaga M,Tumen-Ulzii A,Byuantushig, T, 2024 . The System models of Human body, Lambert
17.Ambaga M,Tumen-Ulzii A,Byuantushig, T, 2024, The molecular mechanism of the the membrane redoxy potential: a three state dependency closed 9-step stepped cycle of proton conductance, Asian Journal of Science and technology, vol.15,Issue,07,pp.13067 -13070.
18.Boyer, P. D. "Energy Capture and Use in Plants and Bacteria. Final Technical Report", University of California Los Angeles. UCLA), United States Department of Energy,. December 31, 1993)
19.Harpers Biochemistry-Twenty second Edition
20.Kulan Ts, Ambaga M, Chimedragchaa Ch, 2016, Effect of Honey Bee venom (Apis melilifera) on Hyperglycemia and Hyperlipidemia in Alloxan induced Diabetic Rabbits, Journal of Diabetes and Metabolism, v.6, p.507
21.Nick Lane, and William F. Martin. 2012. The origin of membrane bioenergetics J.cell, http://dx.doi.org/10.1016/j.cell.2012.11.050.
22.Nick Lane, The vital question. Energy, Evolution and the origins of Complex life) https://en.wikipedia.org/wiki/Biosphere
23. Rubin, E.farber J.L. Essential pathology, second edition
24.Víctor Sojo, Andrew Pomiankowski, Nick Lane, 2014. A Bioenergetic Basis for Membrane Divergence in Archaea and Bacteria, Published: August 12, 2014, http://dx.doi.org/10.1371/journal.pbio.1001926
25.Walker, J. E.; Saraste, M; Runswick, M. J.; Gay, N. J. 1982. "Distantly related sequences in the alpha- and beta-subunits of ATP synthase, myosin, kinases and other ATP-requiring enzymes and a common nucleotide binding fold". *The EMBO Journal,* 1(8): 945–51. doi:10.1002/j.1460-2075.1982.tb01276.x. PMC 553140. PMID 6329717
26.https://en.wikipedia.org/wiki/Thermogenesis
27.https://en.wikipedia.org/wiki/Glycolysis
28.https://en.wikipedia.org/wiki/Brown_adipose_tissue
29.https://www.biologydiscussion.com/biochemistry/lipids-biochemistry/oxidation-of-fatty-acids-biochemistry/72756
30.https://en.wikipedia.org/wiki/Adenosine_triphosphate
31.https://en.wikipedia.org/wiki/Bohr_effect
32.https://en.wikipedia.org/wiki/Haldane_effect
33.https://en.wikipedia.org/wiki/Pulmonary_circulation
34.https://derangedphysiology.com/main/cicm-primary-exam/required-reading/acid-base-physiology/Chapter%20203/buffering-acute-respiratory-acid-base-disturbances

****