

A model for theory-driven research to prove ~~the~~that Electrohomeopathic medicines are nanoparticles and to validate the mechanisms of Electrohomeopathic remedy actions in a complex human system

ABSTRACT:

Introduction: Electrohomeopathy is a herbal-based alternative branch of ~~the~~ medical science which has been projected by Dr. Count Ceasare Mattie of Italy in 1865. Since then it is comprehensively practiced in many countries by ~~the~~ electrohomeopathic practitioners with ~~safe~~safety and success.

Objective: To prove the Electrohomeopathic remedies that are nanoparticles and act by allostatic cross-adaptation, time-dependent sensitization, and balancing the blood and lymph in a complex human system.

Methods: A narrative literature search was conducted by searching ~~in~~ databases including Web of Science, Scopus, Google Scholar, Science Direct, PubMed Central, Elsevier, Springer Link, and many others. from 2001 to 2020 with the following keyword search terms: ~~nanoparticles, electrohomeopathy~~nanoparticles, electrohomeopathy, fluid homeostasis, allostatic network system, etc. All the information ~~secured~~ when searching the database using the above search criteria were assembled, analyzed, ~~and scrutinized in a systemic way~~systemically and repeated articles were deleted. In the final step, to obtain more data, a manual search was conducted using the reference list of the included articles.

Result: This paper suggests ~~a novel~~ model for the Electrohomeopathic remedies are ~~the~~ source of nanoparticles and act by ~~organizing~~ hormesis, time-dependent sensitization, and stabilizing blood and lymph constituents and characteristics (fluid homeostasis) ~~via~~ non-pharmacological but physiological effects on own specific biological adaptive and expanded mechanisms.

Keywords: *Allostatic stress response network, Alternative medical system, Electrohomeopathy, Nanoparticle,*

I. INTRODUCTION

~~Disease~~The disease is the result of harmful deviation from the normal structural or functional ailment of an organism, generally related ~~with~~to certain signs and symptoms other than an injury. The concept for etiology of diseases ~~differs~~differs from one medical science to another. As per ~~the~~ modern medical science, a disease may be caused by external factors such as pathogens or by internal dysfunctions like immunological disorder, metabolic disorder, or ~~may be~~maybe a genetic disorder. The treatment based ~~on~~in modern medicine is purely on ~~the~~ pharmacological action of drugs. According to Ayurveda, all ailments, mental or physical, are caused by the imbalance of the three doshas like Kapha, Vata, and Pitta. Endogenous causes of the disease due to internal variations of the doshas, and exogenous causes due to factors from outside. The Ayurvedic treatment is based on balancing the functions or doshas [1]. As per the Homeopathic concept, the disease is nothing more than an alteration in the state of health of an individual. This is caused by the dynamic action of external, inimical forces upon the life principle of the living organism, known by perceptible signs and symptoms [2]. The homeopathic treatment is a medical system based on two unconventional theories: i) "Like cures like". The concept that a disease can be cured by a drug that produces similar symptoms in healthy people .ii) "Law of minimum dose"—the best possible lower the dose of the drug, the greater its effectiveness.[3]. As per Electrohomeopathy, the disease ~~are~~is manifested due to ~~an~~ imbalance between lymph and blood and the causes ~~whatever~~ may be and that is external or internal ~~and~~ the treatment objective is to balance the blood

and lymph by giving structural specific and functional specific medicines and also based on the temperament of person and law of polarity [4].

The purpose of this paper is to propose a model that explains ~~about~~ the nature of Electrohomeopathy medicines and their mechanism of action on the human system. Basic science research suggests that typically prepared Electrohomeopathic remedies (A) contain remarkable source nanoparticles ~~which that~~ are heterogeneously dispersed in colloidal solution. (B) They act by regulating the biological function of the allostatic stress response network ~~and~~ (C) elicit biphasic actions on the adaptive plasticity of human systems. The effects of Electrohomeopathic remedy nanoparticles relate ~~to~~ state- and time-dependent adaptive changes within the complex adaptive system. The main clinical result is (D) improvement in systemic resilience to future environmental stressors and healing back to normal healthy homeostatic functioning. (E) Electrohomeopathy remedies to balance the blood and lymph of their constituents and characteristics.

2.1. Electrohomeopathy is ~~an~~ complementary alternative medical therapy

Electrohomeopathy is an over 150-year-old system of complementary and alternative medicine (CAM) developed by the Italian Count Cesare Mattie. The field has a well-articulated practice theory, extensive case report-based clinical literature, high levels of patient satisfaction, and a growing modern research base. The typical process of manufacturing of Electrohomeopathic medicines involves ~~cohabitation~~ ~~cohabitation~~ followed by serial dilution in water and succussion [5]. Original bulk-form source materials are typically from plant parts. Count Cesare Mattie pointed out that ~~the living organism is~~ a complex one and the disease can be cured by complex medicines only. So he postulated the concept of is "~~Complexia~~ ~~Complex~~ Complexes ~~Curantor~~ ~~Curator~~"[6].

2.2 Electrohomeopathy nanomaterial remedies are source nanoparticles, not bulk material drugs

There is a chance of ~~the~~ development of top-down nanostructures due to liquid successions ~~or~~ higher successive dilution [9]. Nanoparticles ~~have the ability to can~~ stimulate hormesis, a helpful low-dose adaptive response. [10] If the bulk form source material undergoes repeated dilution followed with ~~succession~~, it may produce gradually smaller and smaller molecules in ~~the~~ true solution until ultimately none should persist in a solution diluted past Avogadro's Avogadro's number (6×10^{23}) [11]. As per their character, top-down manufacturing methods ~~have a tendency to tend~~ to generate variability in sizes, shapes, and structural defects in the resultant nanoparticles. Data shows that the resultant nanoparticles vary in ~~size~~ ~~size~~ and biological effects as a function of the plant sources with which they were originally manufactured. Their biological effects would then differ from those of the "same" material at the bulk form micro level [12]. The repeated dilution and succession procedures in Electrohomeopathic remedy preparation may ~~really~~ be basic manual methods that initiate "top-down" nanoparticles from ~~the~~ bulk source material. The size of nanoparticles may vary from 1 nanometer (nm) to 1000 nm or more. The successions ~~cause~~ turbulence, particle collisions, and shear forces into ~~the~~ solution that further break the remedy source material ~~to into~~ much smaller particles. The combined collision of these mechanical nanosizing processes ~~change~~ ~~changes~~ the properties of original bulk source materials. As the nanoparticles are highly reactive and ~~having~~ ~~have~~ catalytic ~~surface~~ ~~surfaces~~, they could self ~~aggregated~~ ~~aggregate~~ and freely adsorb to other nanoparticles and organic materials onto their surface. e.g., proteins, plant extracts DNA, etc. [13]. Research showed that in vitro, plant mother tinctures are capable of biosynthesizing metal nanoparticles and structures via natural phytochemical reactions. [14]. When plant tinctures are used for ~~the~~ synthesis of nanoparticles, the herbal constituents ~~adsorb~~ ~~adsorb~~ onto the surfaces and ~~changes~~ ~~change~~ the properties of the newly formed nanoparticles [15]. It is difficult to detect and study the characteristics of these particles and proposed nanostructures present in Electrohomeopathy medicines.

especially at higher potencies. However, some devices like atomic force microscopy, and scanning electron microscopy are somehow helpful to identify the presence of nanoparticles in a given remedy [16].

2.3. Mechanisms of Electrohomeopathic remedy actions

Different assumption frames and principles are derived from extensive literature research and are used to demonstrate the mechanism of action of Electrohomeopathy remedies based on the theoretical model. In general in a minimum dose nanoparticles act as biological signals that stimulate the organism's allostatic biological stress response network evoking nonlinear modulatory, self-organizing change. [17]. As the Electrohomeopathy remedies are nanoparticles, it is also assumed that these also mimic the same action by maintaining a harmony between blood and lymph.

Assumption frame: The distinct assumption frame discussion, and divergent principles deliver the theoretical basis for this model. [Figure - 1]

A) Human beings have the ability to adjust to different situations accordingly which is called complex adaptive systems which are interconnected with self-organizing networks [18].

B) The allostatic stress response network of interconnected endocrine, nervous, immune, and metabolic pathways is the central point within the organism that interfaces with the organism to maintain homeostasis. Some exogenous or endogenous stressors disturb the homeostatic balance in the human system. The allostatic stress response network pathways reorganize to environmental stressors [19]. Some of the prominent network pathways are immune, nervous, endocrine, and metabolic networks. Progressive allostatic overload beyond the adaptive capacity of the organism by stressors leads over time to disturb the functional and structural body system and cause disease. The disease is determined by genetic, epigenetic, metabolic, and sedative lifestyle factors and appears as unique complex, nonlinear, dynamical patterns of abnormal function, [20].

C) Continuous allostatic overload by high-level stressors during course of over time leads to the exposure of disease in the organism in a unique complex, nonlinear, dynamical pattern of abnormal function, regulated by genetic and epigenetic factors. [21]

D) Lymph and blood imbalance is one of the prominent causes of disease. The lymphatic or lymph system entails an extensive network of vessels that passes through almost all our tissues to flow a fluid called lymph. Lymph circulates through the entire body in a similar way to blood. The lymph performs three principal functions: Fluid balance, Absorption, and Immunity enhancer. Accumulations of toxins or impurities in the body can lead to toxicity in the blood. As the blood reaches almost all tissues and the lymphatic channel also almost touches all tissue, there is an assumption that the disease is manifested due to an imbalance in the constituent, characteristics, and flow of body fluids especially vital fluids like blood and lymph [22].

2.4. Principle of healing by Electrohomeopathy

2.4.1. Electrohomeopathy nanoparticles elicit a complex adaptive response in the allostatic stress response network.

In this model, it is the stimulus nature of the salient remedy Electrohomeopathic nanoparticles that interrupts the disease-related, dysfunctional allostatic set point and initiates the re-organizing effects on living systems. Electrohomeopathic medicine mobilizes changes in the adaptive plasticity of the biological stress response system (allostasis) [23]. To originate the healing process, the organism has to identify a novel stimulus from the entry of low doses of the salient remedy nanoparticles into the system. The reversal of direction from disease towards health stems from the potentiality of mild doses of nanoparticles to start hormesis, i.e., compensatory

adaptive changes prepare the organism to better resist the already initiated or future adverse effects of the same or cross-adapted stressors. The remedy nanoparticles in minimum dose could bring compensatory changes to reverse the direction of the existed ~~maladaptive~~ maladaptive state, improve well-being, and strengthen systemic resilience.[24]. The selected Electrohomeopathy nanoparticles act in low doses as dynamical biological triggers to modulate several interactive functions in the allostatic stress response network of the organism.

The Electrohomeopathic remedy action is based on different -principles of the nanoparticle-allostatic reverse-adaptation or -cross-adaptation-sensitization-. This model explains-

(A) Electrohomeopathic remedies are highly reactive source nanoparticles and do not contain any original bulk-form drugs

(B) Remedy nanoparticles stimulate a complex adaptive response in the human system -that begins in the different network systems of allostatic stress response ~~indirect~~ indirectly physiologically but not pharmacologically[25]. The Electrohomeopathic -remedy in form of nanoparticles perform as low-level, but highly salient novel stressors and ~~generate~~ generates biological signals for the human system-.

(C) The remedy nanoparticles as very minimum intensity ~~stressors~~ stressors, stimulate changes in the opposite direction to counter the direction of high-intensity ~~stressors~~ stressors which are responsible for the manifestation of the disease [26]. The effect of Electrohomeopathy remedies -on living systems ~~involve~~ involves nonlinear physiological phenomena such as hormesis, cross-adaptation, time-dependent sensitization, and cross-sensitization. -

(D) The complex -adaptive changes that the remedy stimulates -ultimately strengthen systemic resilience [27].

[E] The balance between the constituent and characteristic of blood and lymph is- vital to heal healing the disease.-

2.5. Literature informing model development

2.5.1. Electrohomeopathic remedies are highly reactive source nanoparticles

Nanoparticles -are small- particles with one or more dimensions measuring 100 nanometers or less. Nanoparticles (NPs) have different properties from their bulk forms in terms of mechanical, optical, electrical, magnetic, chemical, biological, and quantum behaviors.[28]. Nanoparticles- do not contain any- original bulk-form drugs. [29].- Their properties, including biological effects, would then differ from those of the "same" material at the bulk form macro level. [30]. If only in terms of improved bioavailability and enhanced effects at a lower dose.[31]. Nanoparticles have altered physical, chemical, biological, optical, electrical, magnetic, and quantum properties that can differ substantially from the bulk forms of the same substance. [32]. Nanoparticles are by nature highly reactive and serve as enhanced drug and herb delivery vehicles which that can reduce the ~~amount~~ number of ~~agent~~ agents needed to achieve a given effect[33]. -As Electrohomeopathic remedies are the source of -nanoparticles -and they also ~~do not~~ do not contain any -original bulk-form drugs,- logically they can perform all the above activities what ~~those~~ that are expected from nanoparticles. - These are highly reactive source- nanoparticles and -act as a very low dose of stressors to organize hormesis and ~~time dependent~~ time-dependent sensitization via non-pharmacological effects on specific physiological adaptive mechanisms may be bringing a balance between blood and lymph both constituency, characteristic- and flow ability. Both topdown physical succussion and plant-essence biosynthesis methods generate the initial nanostructures. The features like structure, morphology, and functional properties are the characteristics by which the Electrohomeopathy nanoparticle remedies -could distinguish them from conventional bulk form drugs.-

2.5.2. Electrohomeopathic remedies stimulate a complex adaptive response in the organism

Human beings are complex adaptive systems with ~~inter-connected~~interconnected and interdependent allostatic stress response networks of nervous, endocrine, immune, and metabolic pathways. A complex self-organizing cluster of constituents that interact with one another and adjust to changes in the environment, i.e., learn, to optimize fitness for survival. The individual as a complex adaptive system is constantly trying to survive as much as possible within his own-world [34]. ~~Successful~~The successful treatment initiates compensatory cross-adaptations that optimize the ability to function as well as possible within the individual's fitness landscape, manifested as resilience to future stress [35]. Remedy nanoparticles initiate a complex adaptive response in the allostatic network with cascading effects that emerge across the entire self-organizing organism over time [36]. The remedy nanoparticles, in a low dose form, trigger the reversal of direction in the pre-established, disease-related maladaptive patterns. The result is improved adaptability to stress, with putting back normal homeostatic function, the rectification of disease, and a developing sense of recovery. The healing process developed as a nonlinear, magnified active adaptive response [37]. As the human system is a complex one and Electrohomeopathic medicines are complex remedies, the selection of a complex remedy to a complex human system is safe, essential, and beneficial. Moreover, due to the nano nature, there is argumentation for the ability of the electrohomeopathy remedy to stimulate a complex adaptive response in the organism and initiates compensatory cross-adaptations.

2.5.3. Electrohomeopathic remedies initiate allostatic stress response network

The immediate interface between the environment and the human system is the allostatic nonlinear stress response network. As per physiology, a stressor is a type of environmental or exogenous stimulus or signal that disturbs the system's homeostasis. The different types of stressors are metabolic, genetic, biological, infectious, chemical, physical, nutritional, electromagnetic, or psychosocial and act as a signal that disturbs the human system's homeostasis. Nanoparticles are lower-intensity stressors that stimulate adaptive plasticity and regulate the system to restore homeostasis.[38]. To facilitate the healing process, the organism has to receive a minimum-dose of the novel stimulus of the salient remedy nanoparticles into the system. [39]. As Electrohomeopathic remedy nanoparticles are lower intensity stressors and capable of initiating a complex adaptive response in the allostatic network. The mediating processes for the remedy results are physiological, not pharmacological. Mediating processes include, hormesis, cross-adaptation, and time-dependent sensitization. So it can be ratiocinated that Electrohomeopathy medicines can stimulate adaptive plasticity and regulate the system to restore homeostasis. In nanoparticle form, remedies would execute these changes by regulating genetic course, as well as the nonlinear dynamical role of physiological defenses in the complex human system, switching from a disease pattern to a healthier recovery pattern.

2.5.4. Electrohomeopathic remedies stimulate hormetic changes

Hormesis is the nonlinear dose-response relationship in which low versus high doses of a given stressor can exercise effects in opposite directions. If an agent can inhibit function at a high dose, then the minimum dose or hormetic dose will stimulate the function; and vice versa. It is an adaptive response of cells of a human system to stress. Types of stressor categories include physical, chemical, biological, and/or psychological factors [40]. It is a biphasic dose-response relationship involving low dose stimulation (beneficial compensatory changes) and high dose inhibition (toxicity); an adaptive response of cells and organisms to moderate intermittent stress[41]. The reversal of direction from disease towards health stems from the ability of low doses of nanoparticles to initiate hormesis, Nanoparticles show the ability to stimulate low-dose adaptive responses (hormesis). Beyond dose, size, shape, and surface charge variations of nanoparticles evoke nonlinear responses in complex adaptive systems [42]. The nanoparticle nature of electrohomeopathy remedies

dialectic its- effects as nonlinear and depends on specific adaptive changes and able to initiate hormosis -in the organism and could- act on physiological but not on specific pharmacological effects of the human- system.

2.5.5. Electrohomeopathic remedies organize Cross-adaptation

Cross-adaptation is a physiological and biochemical phenomenon [43]. -In cross-adaptation, different -types of stressors can disturb the same intermediaries in the allostatic network-. In the current model, the remedy nanoparticles would organize a physiological cross--adaptation response- to the net effects of the previous- stressors that initially- led to the disease state.[44].

The priming and cross-adaptive responses to low--dose Electrohomeopathy remedies or environmental nanoparticles-__also occur in isolated cell systems. The brain is a chief controller hub and coordinatingcoordinates the -allostatic network regulation for the whole organism. Several mediators of inflammatory, endocrine, immune, and metabolic responses correspond bidirectionally with the C.N.S. and with one another to mount an overall homeostatic regulatory response to environmental stressors. There is a reason that Electrohomeopathy nanoparticles serve as a minimum intensity but cross-adapted stressor, advantageous -effects would gradually develop over- course -of time because of pre-existing adaptations to disease-related stressors that the human system -had already developed. Thus the -Electrohomeopathic remedy nanoparticles organize -cross-adaptation within the same allostatic network components that the individual's disease had initially affected.

2.5.6. Electrohomeopathic remedies initiate Time-dependent sensitization

Time-dependent sensitization (TDS) is a form of metaplastic adaptation that produces gradual -endogenous response magnification -with the course ofover time between repeated, recurring stressors. Nanoparticles as minimum intensity stressors for the cells and overall organism would be capable of triggering TDS [45]. Electrohomeopathic remedyremedies in the form of nanoparticles serve as novel minimum stressors corresponding to the organism'sorganism's impaired function and initiate time-dependent cross-sensitization, reversing the direction of dysfunctional reactivity to proper form.

2.5.7. Electrohomeopathic remedies adopt Cross-sensitization

Cross sensitization means one agent begins -and a different agent triggers -sensitized responses. Mild dose nanoparticles act on the disease-primed human system-- as novel physiological stressors reflecting its dysfunction. The result is to elicit magnified, cross-adapted oscillatory changes in the opposite direction to those caused by the disease [46]. That is, the remedy Electrohomeopathy nanoparticles -are cross-adapted, as well as -cross-sensitized to the net disease-based abnormal changes that are initially -established in the human system- at the moment of remedy application.

2.5.8. Electrohomeopathic remedies- stimulate Systemic resilience.

Resilience in a physiological system permits it to reverse to normal function on its own after the-exposure ofto a given environmental stressor. The successfully treated individual can combat -and reverse-from upcoming challenges from higher intensity homeostatic disruptors of the organism as a complex network, at systemic as well as -local levels functional system. The remedy nanoparticles, as a low--level stressor, then trigger a reversal of direction in the prior established, abnormal maladaptive patterns [47]. The more likely it is that the remedy nanoparticles in low dosedoses could evoke compensatory changes to reverse the direction of the existing maladaptativemaladaptive state, improve well-being, and strengthen systemic resilience [48]. Electrohomeopathic medicine consists of nanoparticles-which that act as-low--level stressors ultimately enhancing resilience to higher intensity homeostatic disruptors as a complex adaptive system at the whole organism and local levels of the organization.-_ So it can be debated that the cross-adapted and cross-

sensitized Electrohomeopathic remedy nanoparticles counter the adverse effect of the previous- high--level stressors that initially caused the disease. These act as mild level stressors ultimately enhancing resilience to higher intensity homeostatic disruptors as a complex adaptive system at the systemic level as well as- local levels of the human system. The highly reactive characteristics of Electrohomeopathic nanoparticles can shift the already low hormetic dose-response curve even lower in terms of the dose needed to mobilize adaptive changes. The consequence- is improved resilience to stress, with a bounce back ofto normal homeostatic function and there is a chance for the -recovery- of the disease.

2.5.9. Lymph and Blood Balance (fluid homeostasis)

As most of the cells in the human body are not exposed to the -external environment, the circulatory system acts as a transport system for these cells. Two prominent -fluids move through the circulatory system: blood and lymph. Blood carries oxygen and nutrients to the body's cells, and takes waste materials away. Blood also carries hormones, which control body processes, and antibodies, to fight against invading germs. The lymphatic system (lymph, lymph nodes, and lymph vessels) assistassists the circulatory system by draining excess fluids and proteins from tissues back into the bloodstream, thereby restricting tissue swelling. It also performs as a defense system for the host, filtering out organisms whichthat are responsible for -the disease, producing WBC, and generating antibodies. Injure to the lymphatic and circulatory systems leads the body more susceptible to sickness. Some of the drawbacks of impurity in the blood can bring about diseases like Inflammatory Diseases, Gastrointestinal Complications, -Hormonal Changes, -Impaired Memory, Organ Failure, MalignaeyMalignancy, Autoimmune Diseases, Skin Diseases, etc. [49]. The role of lymph includes fluid balance, absorptive, and immunity enhancer. Lymph- maintains the balance of fluid between the blood and tissues, known as fluid homeostasis It forms -a major part of the body'sbody's immune system and helps defend against bacteria and other intruders. Lymph- enables absorption of fats and fat-soluble nutrients in the digestive system with the help of special small vessels called lacteals. The lymphatic system produces white blood cells, or lymphocytes that are crucial in repulserepulsing infections. Blood and lymph flow side--wise, if there is any abnormality in the blood that may also reflect in the lymph. -So by-balancing--the Lymph and Blood (fluid homeostasis) may overcome the disease and make the person healthy. When blood is unable to -purify itself that time other organs like the kidney, liver and lymphatic system work together to help to purify the blood. There is not any suitable synthetic medication for blood impurities. Only herbal formulations are used for the blood purifier [50]. As Electrohomeopathy system is herbal based, it helps to purify lymph and blood and thus make a proper balance in constituent, eharacteristic-characteristics as well as the flow of lymph and blood properly. The nanoparticles -promptly cross cell membranes and translocate around the body via blood and lymph [51]. As the- Electrohomeopathy remedies are nanoparticles and- it is assumed that they have the ability to cross cell membranes and translocate around the body similarly via blood and lymph. Electrohomeopathic remedies are highly reactive source- nanoparticles that stimulate a complex adaptive response in the organism by correcting the imbalance between blood and lymph constitutionally as well as characteristically physiologically but not pharmacologically. Electro homeopathic remedy nanoparticles organize -cross-adaptation within the same allostatic network components that the individual'sindividual's disease had initially affected perhaps -due to disturbance of blood and lymph harmony.-

3. Conclusion

The proposed model suggests that Electrohomeopathy is logically acceptable, realistic, and unpretentious in the extensive experimental research literature. Electrohomeopathic remedies come into existence and execute their biological effects mainly as nanostructures. They act physiologically but not pharmacologically -probably- by balancing lymph and blood and this -is the most suitable discipline for studying remedy nanoparticle actions.

The Electrohomeopathic medicines consist of nanoparticles which are minimum level environmental stressors physiologically cross-adapted in different degrees to the allostatic overload to which the individual has prior -developed maladaptive responses. The extensive literature on nanoparticles, hormesis, the allostatic stress response network, metaplasticity, and bidirectional time-dependent sensitization can initiate progress in Electrohomeopathic research and the nature of systemic healing. The health researchers would consider this research on logic and rationality as well as –broad-minded thoughtfulness, in evaluating the scientific implications This model provides a rational starting place for an extensive research program on Electrohomeopathic remedy actions. The resultant findings on what Electrohomeopathic remedies are (highly reactive nanoparticles) and how they interact with complex living systems (as pulsed, minimum level doses of a salient and novel environmental stressor) could remarkably advance the field as a precious form of nanomedicine.

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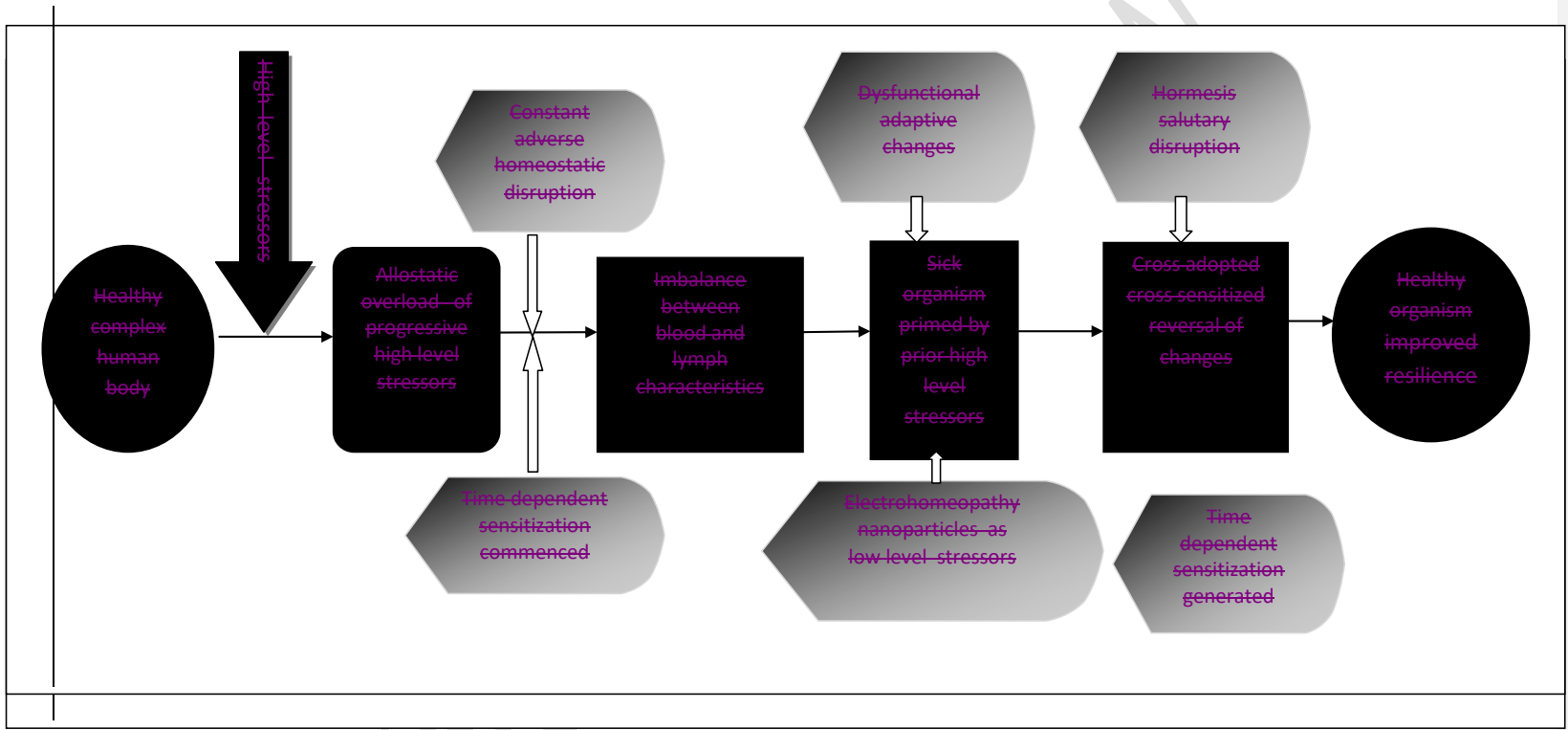


Fig: 1 Nanoparticle – Allostasis – Cross Adaptation – Fluid Homeostasis Model for Electrohomeopathy Remedy Action

UNDER PEER REVIEW