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UNDERSTANDING THE MECHANISM OF ACTION OF POTENTISED HOMOEOPATHIC MEDICINE

Rajaganapathy Lingeswaren [1]

[1] Department of Homoeopathic repertory, Sivaraj Homoeopathic Medical College & RI, Salem, Tamilnadu, India, An Affiliated institute under The Tamilnadu Dr.MGR Medical University, India

Abstract: The Homoeopathic system follows the principle of similia similibus curantur. The concept of potentisation, molecular action of Homoeopathic drug substances, can be explained through an in-vitro study by using Staphylococcus aureus culture. Microbial culture prepared with nutrient agar medium, Hear the bacteria itself considered a whole organism. Nitric acid 1X, 2X, 3X, 4X, 5X, 6X, and 30C as taken as study sample, erythromycin 1X, 2X, 3X, 4X, 5X, 6X, and 30C used as a comparison, water plus ethanol solution used as a negative control. Nitric acid shows inhibitory effects on culture growth up to 3X. Erythromycin up to 5X. Negative control and other dilutions produce no inhibitory effects. There is no growth-stimulating effects or any other effects seen on the culture. A drug in its high concentration produces a group of symptoms during drug proving through its molecular or receptor interactions. Such drugs in their low concentrations follow the same molecular pathway or receptor pathway. We can understand the concepts much better with the action of capsaicin alkaloid on TRPV1 receptor, indications of capsicum annum homoeopathic drug from its drug proving records, Along with that, examples of homoeopathic medicine's active compounds and their molecular or receptor interactions compared with the involvement of such receptors in the disease process. Administration of specific homoeopathic medicine having an affinity towards the particular receptors or molecules involved in the disease process leads to modulation of such receptor or molecular pathway it offers the betterment of symptoms or curative effects.

Index Terms **- Nitric acid dilutions, Erythromycin dilutions, Antimicrobial activity of potencies, Receptor modulation mechanism, Molecular pathway mechanism, Homoeopathic medicine.**

INTRODUCTION

The Homoeopathic system of medicine follows the principle of similia similibus curantur. In this system of medicine, treatment to the patient is with highly diluted medicinal substances. Materia Medica of homoeopathy is constructed based on the concept of drug proving on healthy human beings [10]. Exactly Indicated medicine for the therapeutic purpose selected in the following manner. After the case-taking, the symptoms are compared with symptoms of the drug within the Materia Medica. That indicated medicine contains symptoms identical to the patient's symptoms [10,22,42].

There is much controversy around homoeopathy about the mode of action of homoeopathic medicine. Homoeopathic practitioners use different varieties of potency to treat the patients. Mother tinctures or Mother solutions diluted with distilled water or dispensing alcohol in a serial manner, then by giving a particular number of agitations potencies are prepared. The possibility of getting a single molecule of the original drug is reduced when in higher dilution, for example: above 12C potencies (e.g., 30C = 10^{-60})[10,21,22,42].

In the homoeopathic medical system, three verities of ratios used to make potentised dilutions are 1:9, 1:99, and 1: 50,000. Potentisation is the process of giving a succussion/agitation (downward stroke) to the serial dilution [5,11,21,42]. In earlier periods of the homoeopathic system, low potencies containing original drug substances in high levels to traceable levels, alcoholic extracts of the drugs or solutions made with distilled water called mother solutions used to administer for drug proving [66,67]. Most of the polychrest drugs of the homoeopathic materia medica developed through this kind of drug proving and also with the help of toxicological records [10,22,42].

Hahnemann initially diluted the medicine in different ratios only to reduce unwanted side effects [73]. Later on, he developed the concept of dynamic theory when he tried to explain the modus operandi of homoeopathic medicine, even though he frequently uses it in lower dilution/potency. The principle of dynamisation theory is some immaterial curative power developed in homoeopathic medicine when it is diluted or potentised. It makes contradiction with modern science [66,67].

Data of drug proving on healthy persons, toxicological studies and clinical experiences play a role in understanding the pure pathogenesis effects of a homoeopathic remedy. Pathogenesis effect of drug materials, recorded in homoeopathic materia medica [10,22,42] .

Many drug proving trials and clinical trials show a significant activity of different homoeopathic potencies. Symptoms appearance and disappearance are the basic parameters in clinical and human pathogenic trials [10,22,42]. There is difficulty in understanding the action of potentised medicine on a multicellular living organism such as a human being. In this article, in vitro study model was used to explain the modus operandi of homoeopathic medicine.

Methodology:
Staphylococcus aureus culture mediums are used to design an simple in vitro study model to understand the mode of action of homoeopathic medicine. Staphylococcus aureus is cultured in a nutrient agar medium. An environment (Chennai) sample of staphylococcus aureus strains is collected and identified by the gram staining and sequencing method (sequence ID: K7971132.1). Then it is used to culture the medium.

Nitric acid a homoeopathic medicine taken as a study sample, mother solution (or) 1X of Nitric acid is prepared by adding 100µl concentric nitric acid into the 900 µl of distilled water (1:9 ratio). Preparation of succeeding potencies 2X, 3X, 4X, 5X, 6X, by taking 100 µl of previous potency and 900 µl of distilled water then giving ten-strong succussions. 1000 µl of 30C of nitric acid prepared by dilution (potency) above mentioned method, using a ratio of 10 µl of the previous potencies added 990 µl of distilled water and 100 succussions given at each stage up to 30C potency [7].

Sample of erythromycin taken for comparison, 500mg of erythromycin tablet pulverized to a powder, and 1mg of that powder added with 9ml of distilled water to produce mother solution of erythromycin, further 2X,3X,4X,6X and 30C potency of erythromycin prepared as same as nitric acid. Nitric acid and erythromycin are taken as study samples because nitric acid is a known source of nitric oxide (NO), whereas erythromycin has a strong antibacterial effect [21]. One part of dispensing alcohol, mixed with nine parts of distilled water to produces a negative control sample.

The sample was introduced into the culture medium by the disk diffusion method. Discs impregnated with the installation of 20 µl samples of 1X,2X,3X,4X,5X,6X,30C. Then the discs are placed on the culture plates. Every plate should contain four discs. Then the culture plates are incubated for 24 hours at 37°C. Each study sample has a separate culture plate. After the incubation period diameter of the zone of inhibition is measured.

Results:
Mother solutions/1x, 2X, 3X, 4X, 5X, 6X & 30C potency of nitric acid and erythromycin produce a significant amount of zone of inhibition. Nitric acid shows antibacterial effects up to 3X, whereas erythromycin show antibacterial effect up to 5X potency.
Other potencies of both sample and negative control show no zone of inhibition. And there is no sign of enhanced growth within the culture plates.

Discussion:

Erythromycin is macrolides or ketolides, and it acts as an antimicrobial agent by inhibiting protein synthesis in microbes. Molecules of erythromycin bind with the 50S subunit of the ribosome. Thus inhibit the translocation of amino acids and affecting the synthesis of proteins will disrupt the normal metabolism of bacteria, resulting in the lysis of bacteria cells [52].

Both Higher and lower concentrations of Erythromycin work in a similar molecular pathway where it shows bactericidal effects up to 5x (Table 2) because erythromycins increased affinity towards the 50S subunits of ribosomes [52].

Homoeopathic Medicine Nitric acid 1x, 2x 3x, show antibacterial effects (Table 1) due to the presence of NO and nitrates (NO_3). During agitation/succussion nitric acid (HNO_3) disassociate into NO_3 and nitric oxide ($HNO_3 + H2O \rightarrow NO_3^-$). Nitrates can form in nital solution (Aquas alcoholic + nitric acid solution) [26,50].

Nitric acid is a relatively strong acid that tends to ionize completely in an aqueous solution. The resulting H_3O^+ hydronium ion is the conjugate acid, whiles the NO_3^- (nitrate) is the conjugate base [26,50] . These nitrates and nitric oxide are free radicals, highly lipophilic and they are dissolved in the outer lipid layer of the staphylococcus aureus bacteria then deaminate the bacterial DNA. Through this mechanism, nitric acid potencies 1X, 2X, 3X kill the bacteria [46,53].

Agitation/succession increase the disassociation of HNO_3, increase the kinetic energy of NO_3^- ions and increase the molecular dispersion [26]. Nitric acid shows antibacterial effect up to 3X were as erythromycin show it up to 5X. Erythromycin has a very high affinity towards the 50S subunit of the ribosome [52]. Nitric acid half-life is very low compared with erythromycin [45,46,49,50].

The theory of hormesis says high concentration inhibits and low concentration stimulate. In this study, we can't observe growth enhancement in the culture plates [18], administered with ultra-low concentrations of medicines such as 6X, 30C. Hormesis effect may be possible if dilutions of a drug are below ultra-high dilution (containing traces of original drug molecules) and above its inhibition concentration [60,73], such as in nitric acid below 4X and above 3X, in erythromycin below 6X and above 5X. What a pharmacologically active substance does on the physiological system in its high concentration, that kind of activity continued even in its diluted level [12,73] may be up to 12X according to its molecular interactions with the cell.

Nitric oxide is generated in tissues from arginine by nitric oxide synthase (NOS). Inducible NOS is Ca^{++} independent and induced by endotoxins of bacteria and cytokines in macrophages, endothelium, and smooth muscles. The constitutive NOS (cNOS) is a chief component for the production of endogenous NO physiologically [45].

NO is a known agent for the maintaining integrity of the gastric epithelium, diffuses freely across cell membranes. In a biological system, the half-life of NO is less than 30 seconds. Compared with other free radicals, it is less reactive in nature and cannot react with itself. NO works as a physiological messenger through the production of cGMP by activating guanylate cyclase. NO transported to the target cell because of the interaction of NO with Thiol groups. Nitrosylation process of thiol proteins involved in remodelling of the axon terminal [35 ,45].

In oxidative stress, there is an increased synthesize of NO by iNOS. NO reacts with superoxide (O_2^-) and produce peroxynitrite ($ONOO^-$) and hydroxyl radical. They are more toxic than NO. NO is a non-adrenergic, non-cholinergic molecule that acts as a double-edged neurotransmitter as a protective agent and cytotoxic agent [46,49,54].

Protective effects of NO is by regulation of neural transduction through retrograde influence over the release of stimulating neurotransmitters. Cytotoxic effects of NO are due to free radical formation. NO has a half-life of fewer than 6 seconds in the gut lumen, were converted into nitrite and nitrate due to the presence of water and oxygen. It is highly diffusible in water, lipids and also in the air, freely traverses cell membranes through the ways it reaches the adjacent target cells [45,49,50].

NO participates in intestinal water transportation by acting on the epithelium, increasing blood flow, and also it does this by indirectly stimulating neuronal reflexes and interactions with other agents. Activation of soluble guanylate cyclase by NO leads to cGMP formation is a potent activator of intestinal secretions, also act as an inhibitor of gastric acid secretion. NO plays a chief role in protecting gastrointestinal mucous from different types of noxious stimuli through increasing mucosal perfusion. NO acts as a secretomotor neurotransmitter in response to serotonin. Its low concentrations protect B lymphocytes from viral infection. High concentrations of NO stimulate apoptosis in hepatocytes macrophages, glial cells, neurons and other immune cells. Gastric acid secretion in anaesthetized and conscious rats increased by the injection of NO donors centrally. NO also activates vasoactive intestinal polypeptide in secretomotor neurons. These are some examples of contradictory actions of NO [25,45,46,50] .

Studies related to the healing of cutaneous wounds describe that NO enhances collagen production by stimulating fibroblasts. The potential of nitric oxide to form nitrosamines leads to mutation, which facilitates carcinogenesis. NO causes Damage to the DNA by inhibiting its repair mechanism. So NO is a double-edged sword its benefit and detrimental action depend on its local concentration [38, 49].

NO protects the cells from apoptosis, and in contrast to its protective activity, this also induces apoptosis. It facilitates the formation of ONNO by reacting with superoxide anions, which leads to an increase in the membrane permeability and calcium concentrations, through which it stimulates apoptosis. Activation of NO by Bcl-2/Bcl-Xl causes inhibition of the Bax / Back pathway, thereby blocking the caspases cascade. NO inhibits apoptosis by modulating transcriptional factors AP-1, NF-KB and extra cellar singles similar to TNF. So it regulates apoptosis by inhibition of apoptosis in oxidative stress as in mucosal injury and induces apoptosis in carcinogenesis [45,46,50].

There is impaired NO release in diseases like non-relaxing sphincters, infantile hypertrophic pyloric stenosis, achalasia, Hirschsprung disease. In ulcerative colitis appearance of toxic megacolon, overproduction of NO in the colonic smooth muscles may become the cause of this condition. An in vivo study on diabetic rates shows gastrointestinal dysfunction caused by declining tissue L – arginine content and low NO production. Motility disorders such as chronic intestinal pseudo-obstruction, constipation may relate to the enteric NO system [45].

Mother tinctures, low potencies used in drug provings of homoeopathy, most of the polychrest drugs of homoeopathy proved in such way. Example materia medica pura and encyclopedia of pure materia medica, Herrings guiding symptoms of our material medica contains provings of nitric acid in mother solution, 2X, to 12X potencies (Table 3). Homoeopathic drug proving record shows the oral administration of an aqueous solution of nitric acid and its low concentration (low potency) for several days in provers leads appearance of symptoms like inflammation of gums, glossitis, aphthous ulcer, gastritis etc, among the drug provers [69,76].

In the homoeopathic system of medicine, potentised or diluted form of nitric acid is used to treat the conditions like gingivitis, aphthous ulcers, gastritis, and stomach ulcers. Nitric acid potencies produce curative effects on the disease conditions in a single dose or with a few repetitions in particular intervals for a few days. The classical literature of homoeopathy flaunts the use of low potency such as 3X, 4X, which contains the original molecules of nitric acid [70,72,75,76].

The modus operandi of homoeopathic medicines can be explained, with the antibacterial effects of nitric acid and erythromycin in different potencies from this experiment. Based on this study, we can create a hypothesis that is, In which path a higher concentration of pharmacologically active substance acts on the physiological system it continues that path even in the potentised or diluted level where the traceable amount of original molecule present possibly up to 12C. We can observe this phenomenon in Capsicum annum by its active principle capsaicin and its interactions with the TRPV1 receptor [37]. Capsicum annum therapeutically used in homoeopathy [70,75].

There is an expression of a particular group of receptors in tissues or organs involved in the respective kind of disease. For example, in mammals, the TRPV1 receptor is distributed in the unmyelinated C-type sensory nerve fibres and partially present in less myelinated Aδ type of sensory nerve fibre. This receptor also presents in the peripheral nervous system, especially in dorsal root ganglion, trigeminal ganglion vagal ganglion, and other small neurons. The TRPV1 receptor, expressed in the thalamus, striatum

amygdale and other regions of the central nervous system. The Pancreas, liver, lung, heart, GI organs, oral cavity, smooth muscles of the human body also contains this TRPV1 receptor [24].

TRPV1 receptors get activated or sensitized directly or indirectly by different physical, chemical factors, inflammatory mediators, for example, mechanical stimulation, ethanol, inflammatory mediators, tissue damage, noxious heat stimulation that is > 43°C, acid pH less than 5.3, intracellular redox state, changes in extracellular osmotic pressure, substance P (SP), Prostaglandins and nerve growth factor (NGF) [1].

Stimulation of TRPV1 lead to an influx of extracellular Ca_2^+, increased intracellular calcium level causes depolarization of nerve cells to produce an action potential. There is a transmission of an action potential along the sensory nerve fibres of the nerve centre or activation of a series of signalling pathways in the cells, which triggers a wide range of cellular responses. Activation of TRPV1 in sensory nerve fibres causes the release of neuropeptides from the local vesicles, and there is the formation of independent action potential that causes increased terminal calcium in the nerve cells. Through these mechanisms, TRPV1 receptors regulate the corresponding physiological and pathological functions [24].

Capsaicin can stimulate the TRPV1 receptor. It leads to the excitation of TRPV1 followed by the release of neuropeptides. It depends on the capsaicin concentration. Generally, the capsaicin molecule action on the TRPV1 receptor produces pain sensations like burning and heat [24]. The purified capsaicin also has analgesic properties [51,61]. It causes analgesic effects in disease conditions such as intermetatarsal neuromas, lateral epicondylitis and end-stage osteoarthritis. The activity of capsaicin upon the pain modulation TRPV1 receptor is the cause of such analgesic effects. There is blocking of axoplasmic transport of somatostatin, substance P, and the resulting depletion of neuropeptides [37].

TRPV1 regulate gastric acid secretions. A small dose of capsaicin activates the primary nociceptive neurons leads to the release of a large amount of calcitonin generated peptides (CGRPs). This CGRP inhibits irritations caused by gastric acid and pepsin secretion. In a study where oral administration of capsaicin to rats shows acute erosive gastritis [37]. This inflammatory effect is due to the action of a large amount of capsaicin [24]. In homoeopathy, gastritis and its associated symptoms produced by capsicum annum in drug provings, recorded under the respective drug in homoeopathic materia medica records [75,76].

Stimulation of TRPV1 inhibits gastric acid secretion by increasing gastric blood flow and stimulates gastric mucosa to secrete prostaglandins and epidermal growth factors. Through this mechanism, it helps in the healing of gastric ulcers [71]. A study related to functional dyspepsia shows increased dyspeptic symptoms scores after taking the capsicum through the capsule. This study indicates the involvement of the capsaicin receptor channel in functional dyspepsia. The dyspeptic score increased because of the increased visceral sensitivity caused by increased stimulation of TRPV1 [30].

Capsaicin molecule has a higher level of affinity towards the compounds containing SP present on the membrane of sensory nerve terminals. CGRP is an inflammatory, pain-inducing afferent neurotransmitter found in capsaicin-sensitive afferent nerve fibres [24]. Drug proving data in homoeopathy contains records of dyspeptic symptoms caused by ingestion of capsicum mother tincture in significant quantity for several days in healthy drug provers [70,75].

Inflammatory bowel syndrome (IBS) has visceral hypersensitivity caused by increased signal transmission between dorsal horn neurons and the brain. It is one of the chief mechanisms for the formation of pain sensation in IBS. Upregulation of TRPV1 fibres in colon tissue of patients with IBS leads to abdominal pain. PLC/PKC signalling pathway also involved in IBS, it leads to activation of histamine 1 Receptor (HRH1) through histamine-mediated metabolites activation or histamine [24].

In a randomized controlled clinical trial, there is ingestion of capsaicin by patients with IBS causes desensitization were chilli ingested for six weeks that is 2mg of capsaicin per day it reduces the bloating caused by spicy meals and abdominal pain when compared with placebo [6]. In the respiratory system, activation of TRPV1 causes increased intracellular Ca_2^+ concentration leads to excitation of nerve cells followed by secretion of tachykinin CGRP in nerve terminals. These mediators' acts on mucinous gland cells, cholinergic neurons, inflammatory cells, vascular smooth muscle cells (VSMCs) of the trachea in the respiratory tract. It leads to bronchoconstriction, tracheal mucosal oedema, inflammatory cell

chemotaxis, mucous secretions. This kind of TRPV1 activated airway inflammation is a neurogenic inflammation. Airway inflammation caused by activation of TRPV1 leads to pro-inflammatory cytokines, TNF-α, prostaglandin E2, Interleukins and NGF release from the bronchial epithelial cells. Hyper-regulation of TRPV1 also involves cough and Airway hyperresponsiveness [16].

Stimulation of TRPV1 receptor in nasal cavity leads to TRPV channel hyperresponsiveness, stimulation of afferent nerve fibres cause increased glandular secretion, vasodilatation, and increased vascular permeability like in symptoms of chronic rhinitis. Continued capsaicin stimulation leads to a decrease in mucosal permeability, hypo sensitiveness of sensory neurons of the nasal cavity. So these cells become less hyper-reactive through this mechanism neurogenic pains get reduced. Hear SP store depletion leads to desensitization caused by depletion of 4, 5 -bisphosphate PIP2, phosphatidylinositol [37].

In homoeopathic materia medica, we can find the effects of capsaicin through a drug proving of capsicum annum on healthy human beings. Symptoms produced here are identical to the pharmacological effect of capsaicin. Symptoms of a drug produced during drug provings are similar to its pharmacological records (Table 3). Because of the pharmacologically active ingredient or biologically active ingredient present in that drug, its affinity towards the particular receptor or molecular pathway, for example, the interaction of Strychnine with glycine receptor (Table 3). Capsicum annum in homoeopathic materia medica has indications related to the gastric ulcer, IBS, airway hyperresponsiveness based on its drug proving [70,75]. Patients with IBS, cough, airway hyperresponsiveness, functional dyspepsia, treated homeopathically with oral administration capsicum annum in low potency where there is the involvement of TRPV1. Followed by the betterment of symptoms due to downregulation of TRPV1 or reduction in TRPV1 receptor expression, this may happen when low potency of capsicum annum do administer repeatedly [15].

There is no clear definition for the concept of minimum dose in homoeopathy. The least possible quantity of medicine is sufficient to cure it is the explanation for the minimum dose. This minimum dose concept creates confusion among homoeopathic practitioners [65,66]. Earlier homoeopathic practitioners practised with low potencies [23]. That kind of potency has at least traceable amounts of active ingredients. According to the above-explained receptor-mediated or molecular mediated action principle, the minimum dose is nothing but the least quantity of medicine that stimulates or interact with the receptor or molecular pathway. Single doses of medicinal substances in reasonable amounts or repeated administration of low potency at frequent intervals can interact with the receptors or molecular pathway if that potency or dilution contains an original drug molecule, at least in a traceable quantity. To achieve this, we should alter the dilution ratio such as 1:5. It will give more choice of potency with actual drug molecules. There is no strong logic behind the current dilution ratio of homoeopathy [73]. Even Hahnemann practised with dilutions or potencies prepared with different ratios [65,66].

The dynamic theory of Modus Operandi of homoeopathic medicine proposed by Hahnemann is similar to that of receptor pathway mediated or molecular pathway mediated mechanism. Example activity of capsaicin on TRPV1 receptor is identical with the theory of Primary action of the medicine upon the vital force [68]. The reactions that happen after the activation of the TRPV1 receptor is similar to the secondary curative action in homoeopathy [68]. That is the action of a Vital force against the medicinal action.

Hahnemann used the word dynamic because there were no scientific instruments [42] to understand the biological concepts at the microscopical level. But he traces some patterns of action and reaction by observing symptoms of drug provers and patients. So he named it as dynamic action or action of vital force.

In modern times we have scientific instruments for analysing the biological concepts at microscopical levels form this analysis, we know that any action or reaction in a physiological system happens only with the involvement of a specific molecular mechanism.

Table 1: Antibacterial activity of different potencies of Nitric acid in staphylococcus aureus culture (disc diffusion method)

Cultured organism	Nitric acid							Negative control (water + dispensing alcohol)
	Potencies							
Staphylococcus aureus culture	MS/1X	2X	3X	4X	5X	6X	30C	0
	11mm	8mm	6.6 mm	0	0	0	0	

Table 2: Results of Antibacterial activity of different potencies of Erythromycin in staphylococcus aureus culture (disc diffusion method)

Cultured organism	Erythromycin							Negative control (water + dispensing alcohol)
	Potencies							
Staphylococcus aureus culture	MS/1X	2X	3X	4X	5X	6X	30C	0
	17mm	14mm	11mm	9mm	7mm	0	0	

Table 3: Comparing biological activity of the active ingredients of Homoeopathic medicines, their respective receptor interaction or molecular pathway and involvement of such receptor interaction or similar kind of molecular pathway in disease condition, symptoms of Homoeopathic medicines derived from drug proving and potencies of commonly used in homoeopathic practice especially in the earliest period of homoeopathic history.

Sl.No	Name of the Medicine	Active principle/ compound	Receptor Modulation/ Molecular pathway of Active principles of Medicine	List of disease conditions were Similar Receptor or molecular pathway involved.	Drug symptoms form homoeopathic material medica	Potency/ dilution frequently used --- (from homoeopathic classic litteratures)
	Acid Nitricum	Nitric oxide (NO) [69,76]	Nitric oxide is generated in tissues from arginine by nitric oxide synthase (NOS) [45]. NO works as a physiological messenger through the production of cGMP by activating guanylate cyclase [35,45]. Cytotoxic effects of NO are due to free radical formation. The formation of ONNO by reacting with superoxide anions, which leads to an increase in the membrane permeability and calcium concentrations, through which it stimulates apoptosis [45,46,50].	In ulcerative colitis appearance of toxic megacolon, overproduction of NO in the colonic smooth muscles may become the cause of this condition. Gastric ulcers, Motility disorders such as chronic intestinal pseudo-obstruction, constipation may relate to the enteric NO system [45].	Erosions and ulcers of stomach. Abdomen distended with flatus, very tender. Chronic intestinal catarrh. Ulcers in ileo-cecal region. Lower part of abdomen distended, hard and painful to touch. Ulcer on tongue. Ulcerated and blistered lips [69,76].	1X to 6X & 1C to 6C [15,23].
	Aconitum nephalus	Aconitin [13,20,39]	It is a Cardio toxins and neurotoxins. Gastrointestinal involvements. Acts on the voltage-sensitive sodium channels of the cell membranes of excitable tissues, including the myocardium, nerves, and muscles [4]. Bind with high affinity to the open state of the voltage-sensitive sodium channels at site 2, thereby causing a persistent activation of the sodium channels, which become refractory to excitation. The arrhythmogenic properties of	Myotonia and muscle weakness caused by uncontrolled repetitive muscle fiber discharges. Neuro muscular disorders. Epilepsy, long QT syndrome cardiac arrhythmias [27]. The pathological upregulation of Sodium sensitive voltage channels can make cancer cells highly invasive. Impaired cognitive performance [4].	Drawing and paralytic stiffness in right upper arm. Cramplike pain. Oppression especially in region of heart, anxiety in cardiac region, and oppression of chest, with contracted pulse and constriction of the chest. Palpitation, with great anxiety, difficulty of breathing, and great weariness in all the limbs; Dulness	Mother tinctures, 1X to 6X, 1C to 12C [15,23].

			aconitine are in part due to its cholinolytic or anticholinergic effects mediated by the vagus nerve [20].		and confusion of mind. Pulse strong, full, and quick. Rheumatic pain in the nape, felt only on moving the neck. Delirium, Convulsions, Cramps in calves, also in feet. Legs and feet feel numb [31].	
	Agaricus muscarius	Ibotenic acid and Muscimol [63,78]	Muscarine is a selective cholinergic agonist [2]. Activation of this receptor leads to reduced heart rate, lowering of blood pressure, vomiting, diarrhoea, bradycardia, bronchorrhea, tearing, bronchospasm (asthmatic-like breathing), salivation, pupil contraction and blurred vision[55,19]. Muscimol is a non-selective GABAA receptor agonist [3]. Ibotenic acid is an agonist of glutamate receptors [63,78] ,specifically at both the N-methyl-D-aspartate, or NMDA, and trans-ACPD receptor. These agents act as neurotransmitters in the CNS, stimulating glutamate receptors. Confusion, dizziness, tiredness and visual and auditory perceptual changes [47,43].	Epilepsy, ADHD [56], Parkinsons disese, Stroke, Schizophrenia, autism spectrum disorder, and major depressive disorder [58,79]. Acute CNS injury syndromes such as hypoxia-ischemia, trauma, and status epilepticus [57]. Hyperactivity of glutamatergic transmission believed to underlie anxiety disorders [58]. Excessive activation of NMDA receptors causes neuronal injury. Although activation of NMDARs has been proposed to contribute to the progress of diabetes. Endogenous glutamate aggravated β-cell dysfunction. Excessive Glutamate excitotoxicity causes neuronal dysfunction and degeneration [47,36].	Dulness almost amounting to idiocy. Indisposed to perform any labor, especially mental. Anxiety, Epilepsy, Chorea. Constant dizziness. In skin pricking as from needles on different places. Electric stitches, stitches as from splinters ; corroding biting ; itching, burning, biting, stinging sensations. Constant desire to urinate. Quantity of urine very much increased, even with diarrhœa [31].	3X,3C,4C, In skin affections and brain exhaustions lower attenuations indicated [15,23].
	Alumina	Aluminium	Aluminum is a widely recognized	Alzeimer disease,	Consciousness of his	3X to 6X, 3C to 6C

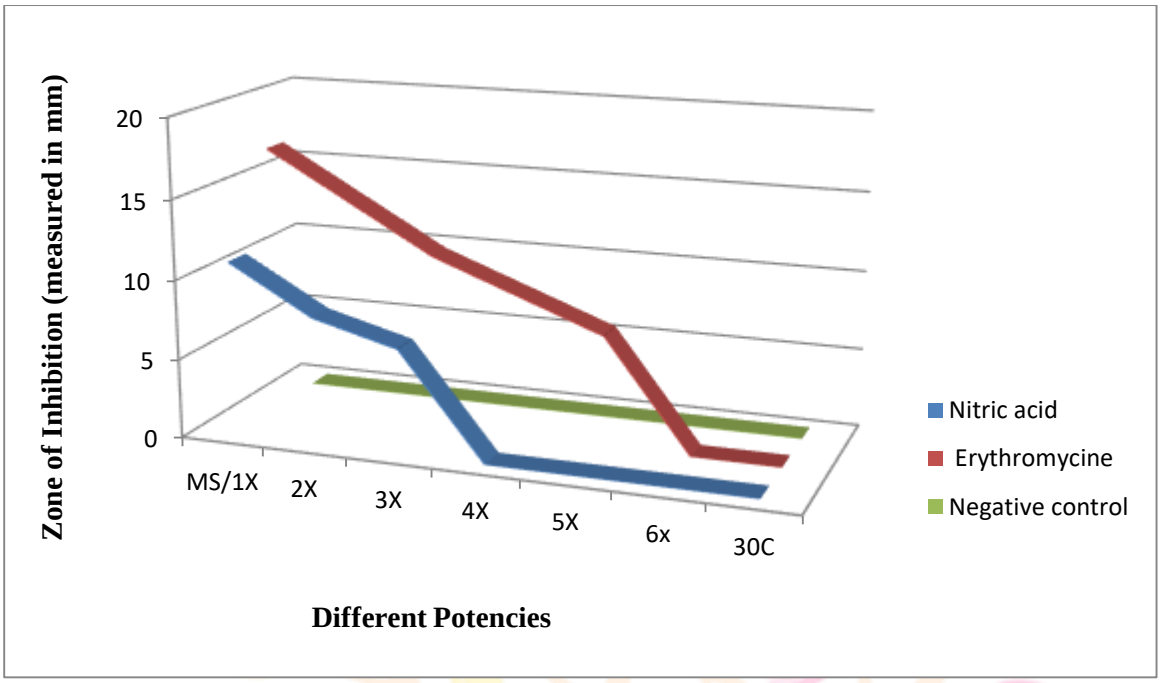
		oxide [31]	neurotoxin that inhibits more than 200 biologically important functions and causes various adverse effects in plants, animals, and humans. Binds to histone-DNA complex and induces conformational changes of chromatin. Induces expression of pro-inflammatory genes and pro-apoptotic genes. Induces elevated expression of APP. It causes neurofibrillary degeneration, inhibits the activity of glucose-6-phosphate dehydrogenase. Aluminium oxide also cause mitochondrial dysfunction and depletion of ATP [44].	Perkinson's disease and diseases with Lewy body.Type 2 diabetes mellitus [44].	personal identity confused. Paralysis. Great weakness or loss of memory. Inability to recollect things or follow up a train of thought. Confusion and obscuration of intellect. Locomotor ataxia. Tremulousness, when he touches anything, he feels electrified. Tremor. Involuntary movements of single parts. Spasms. Slow tottering gait. Frequent micturition. Frequent urination at night [31].	[15,23].
	Arsenicum album	Arsenic Oxide[32]	Arsenic produce toxicity by inactivating up to 200 enzymes, especially those involved in cellular energy pathways and DNA synthesis and repair [64]. Acute arsenic poisoning leads to nausea, vomiting, abdominal pain, and severe diarrhoea. Encephalopathy and peripheral neuropathy. Chronic arsenic toxicity results in multisystem disease. Arsenic is a carcinogen affecting numerous organs. It inhibits the complexes I, II, and IV of the electron transport chain, which elevate mitochondrial production of reactive oxygen species [59].	Diarrhea. Hyperkeratosis. Changes in Pigmentation [59]. Mitochondrial damage has been implicated in the pathogenesis of several neurodegenerative diseases [29].	Itching of skin. Skin dry and scaly. Skin very white and pasty-looking, later yellow, scaly. Psoriasis guttata. Tettery, crustaceous eruption. Gangrene . black eruption. Anemia. Great emaciation, clay-colored face, blue margins around eyes, great weakness of all limbs, want of disposition to do anything and constant inclination to rest ; diarrhœa ; sometimes	2X,3X.3C to12C [15,23]

					dry, hacking cough and night sweats. Emaciation, with want of appetite, or rather aversion to food. Obstinate constipation[32].	
	Atropha belladona	Atropine, scopolamine. Anticholinergic alkaloids [13,39].	Atropine is a competitive muscarinic acetylcholine receptor (mAChR) antagonist [9,41,62]. In the heart, atropine blocks the inhibitory effect of ACh on heart rate and contractility, potentially also leading to tachyarrhythmias[62]. COPD, Asthma [17].	Bronchoconstriction or bronchospasm. Diverticular disease. Chronic obstructive pulmonary disease (COPD) [2]. Atrial tachycardia, fibrillation [77].	Expectoration of viscid and whitish mucus. Catarrh, with cough, coryza, and the head and eyes severely affected. At times expectoration of blackish, thick mucus. Respiration short, hurried, sometimes much oppressed.Difficult respiration. Very frequent small stool; one evacuation is hardly finished before an urging is felt for another. Small, loose stools, with sharp, stitching pain above the umbilicus. Pulse full and quick. Pressing pain in the chest with shortness of breath, and at the same time between the scapulæ, in walking and sitting [32].	Mother tincture, 1X to 12X & 1C to 12C [15,23]
	Capsicum	Capsaicin [38]	Capsaicin interacts with TRPV1	TRPV1 expressions seen	Heartburn, .Gastralgia,	Mother tinctures,

	annuum		receptor. The capsaicin molecule action on the TRPV1 receptor produces pain sensations like burning and heat. TRPV1 regulate gastric acid secretions. Acute erosive gastritis occurs when administration of large doses of capsaicin. Activation of TRPV1 causes increased intracellular Ca_2^+ concentration leads to excitation of nerve cells followed by secretion of tachykinin CGRP in nerve terminals. These mediators' acts on mucinous gland cells, cholinergic neurons, inflammatory cells, vascular smooth muscle cells (VSMCs) of the trachea in the respiratory tract [30,71,6].	in gastric ulcer, functional dyspepsia, oesophagitis. Airway inflammations, asthuma, Inflamatory mega colon, toxic mega colon [1,16].	Accumulation of mucus and acids in stomach. Burning or cutting pains in abdomen. Violent tenesmus. Mucous diarrhœa with tenesmus. Dysentery. Asthma. Nervous, spasmodic cough. Frequent dry, hacking cough [70,75].	1X to 6X, 1C to 12C [15,23]
	Lycopodium	Huperzine A (HupA). Lycopodine.[43]	Inhibitors of acetylcholinesterase (AChE) trigger apoptosis by modulating 5-lipoxygenase [14]. Depolarizing mitochondrial membrane potential. In refractory prostate cancer cells without modulating p53 activity [14]. Lycopodine inhibits proliferation of HeLa cells through induction of apoptosis via caspase-3 activation [48].	Inhibition of acetylcholinesterase seen in conditions like, Constipation/gastroparesis, Memory problems, Difficulty with word recall when speaking, Learning difficulties, Orthostatic hypotension, Low muscle tone, Depressed mood, Fast heart rate, Chronic inflammation, Emotional instability [43,74].	Great loss of memory, Speaks wrong words and syllable. He is unable to read, because he does not recognize and confounds letters. Very sad mood, with confusion of the head. Alzheimer's disease, symptoms of dementia. A hard stool, only after great pressure [33].	Mother tinctures,1X to 12x,3C to 12C [15,23].
	Nux vomica	Strychnine and Brucine [39].	Strychnine interacts with glycine receptors. Strychnine is a competitive antagonist at inhibitory neurotransmitter glycine receptors in the spinal cord, brain stem, and higher centers. It	Myoclonic disorders, Muscular spasms, Conditions were increased muscular activity of the small intestine [28].	Great reflex excitability. Slightest touch of hand immediately brought on spasms. Stitches through body in jerks,	1X to 6X & 1C to 12C [15,23].

			increases neuronal activity and excitability, leading to increased muscular activity. Brucine is a allosteric modulator at cloned M(1) muscarinic receptors. Strychnine poisoning can generate anxiety, backache, enhanced reflexes, equilibrium disorders, heightened sense perception, pain, and stiff neck, then convulsions, dyspnea, and twitching [10,40,80,81].		feels sore all over, < mornings. Violent, contractive, painful sensation through whole body. Severe clonic spasms. Cervico-brachial neuralgia, neck stiff. Rheumatism of muscles of neck, with or without tearing, drawing pains ; head generally drawn to one side and moved with great difficulty. Diarrhœa [15].	
.	Veratrum album	Hypotensive ester alkaloids and Jervine [39].	Veratrum alkaloids increase the permeability of neuronal sodium channels, causing them to fire continuously; increased stimulation of the vagal nerve results in the Bezold–Jarisch reflex, causing hypotension, bradycardia, and apnea [8].	Bradycardia, Ventricular arrhythmias [82].	Palpitation, with anxiety, and rapid audible respiration. Pulse very small, irregular, at times intermittent. Pulse imperceptible. Pulse very slow, even while walking [34].	Mother tinctures, 1X to 12X & 1C to 12C [15,23].

Figure 1: Comparison of antimicrobial activity of different potencies of Nitric acid, Erythromycin and Negative control. Nitric acid shows antibacterial effects up to 3X, whereas erythromycin show antibacterial effect up to 5X potency. Other potencies of both sample and negative control show no zone of inhibition.



Conclusion:

Based on this study and its discussion, a theory can be postulated on the action of homoeopathic medicine, i.e., abnormal sensations and symptoms (disease) caused by stimulation or involvement of a specific receptor or molecular pathway. These receptors or molecules may be stimulated or suppressed by environmental, natural or artificial agents. In such conditions, administration of specific homoeopathic medicine having an affinity towards the particular receptors or molecules involved in the disease process leads to modulation of such receptor or molecular pathway; it can cause the betterment of symptoms or curative effect. This kind of receptor or molecular-based activity of homoeopathic medicines is caused by the presence of biologically or pharmacologically active substances present in that medicines and by their concentrations. For example, belladonna has atrophin, nux vomica has strychnine, digitalis has digoxin, magnesium compounds like magnesium phosphate, magnesium carbonate. Extracts, solutions and low potencies, such as mother tinctures, 1X,2X,3X up to 12X contain quantifiable to traceable amount of the original drug molecule. Homoeopathic physicians of earlier periods used low potencies for therapeutic purposes. It facilitates the success and fame of the homoeopathic system of medicine at that time.

Rational acceptance of concepts of homoeopathy in the light of modern scientific phenomena such as receptor pathway or molecular pathway mediated mechanism of homoeopathic medicine in low potency may strengthen the homoeopathic system scientifically along with that it opens a new opportunity to include new drugs from synthetic origins into homoeopathy as well as new routes of administration such as intramuscular, intravenous administrations. These advancements can create homoeopathic practice reliable and more beneficial to humankind.

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