ISSN : 0974-7168

E- ISSN : 2320- 7094

Volume 11 / Issue 3 / July-September 2017

Indian Journal of Research in Homoeopathy

IJRH

Official Publication of Central Council for Research in Homoeopathy

www.ijrh.org

Medknow

Wolters Kluwer

Review Article

An overview of research at University of Kalyani in exploring some basic issues of Homoeopathy

Anisur Rahman Khuda-Bukhsh*

Department of Zoology, University of Kalyani, Kalyani, West Bengal, India

Abstract

Homoeopathy has been confronted with certain major issues such as (i) how is medicinal property of homoeopathic drug transferred to and retained by the vehicle; (ii) how can it act in biological system in the absence of any original drug substance in ultra high diluted remedies? and (iii) plausible mechanism and pathways of biological action including mysteries of 'like cured by likes'. We demonstrated through controlled studies the ability of ultra-highly diluted homoeopathic drugs in rendering protection/repair of cytogenetic damages inflicted by whole-body X-irradiation in mammalian model mice *in vivo*. We examined cytogenetic damages in arsenic, cadmium, mercury and stannum intoxicated mice and their remediation by homoeopathic drugs derived from agitated ultra-high dilutions of their respective salt, deploying many scientific protocols. We made a human trial on efficacy of *Arsenicum album* against groundwater arsenic-contaminated victims. We tested efficacy of some homoeopathic remedies in cancer of mice and thalassemia in human. We produced nano-capsules of homoeopathic mother tinctures and their bioactive components and induced nano-precipitation of silver from silver nitrate by homoeopathic mother tinctures and characterised them for their physicochemical properties and biological action. We studied tissue distribution of nanoparticles, precise mechanism and pathways of their action that involved certain signal proteins and their pathways, both *in vivo* and *in vitro*. This approach made a significant contribution towards elucidating the role of drug nanoparticles in inducing 'memory of water' and mechanism and pathways of action of homoeopathic remedies through epigenetic modifications that supported 'gene regulatory hypothesis'.

Keywords: Gene regulatory hypothesis, Memory of water, Nano-capsules, Nanoparticles

Introduction

Acceptability of Homoeopathy is mainly challenged when the ultra-high dilutions at or above 12C (diluted 10^{-24} or higher) of remedy are used, because at these dilutions, the remedies are unlikely to contain even a single molecule of the original drug substance, and therefore, their efficacy as medicine becomes an object of suspicion. Non-believers/rationalists argue that the reported clinical effects of such highly diluted remedies may only be 'placebo' or 'psychosomatic effects'. Major questions asked are as follows: (i) Whether it is possible to transfer medicinal property to water or aquatic ethanol (vehicle) by homoeopathic method of serial dilutions with agitations, and if it is, how can it be accomplished? (ii) How can these ultra-highly diluted remedies bring about spectacular physiological changes when these are administered to patients in absolutely micro-doses? (iii) If the remedies can really have remedial effects, then what could be the precise mechanism of their biological action? Our works are mostly related to answering questions 'ii and iii' though they also have bearing on understanding the issue raised in 'i' as well, to some extent. And finally, since homoeopathic practitioners treat patient's symptoms in totality including mind – symptoms in human, based on the dictum 'like cures like', the mystery of similia and mind–body relationships associated with this kind of remedy must also be scientifically addressed.

Our early works

Our initial research works were focussed on proving efficacy of ultra-highly diluted homoeopathic drugs in mammalian model mice (*Mus musculus*) which have the closest similarity

***Address for correspondence:** Dr. Anisur Rahman Khuda-Bukhsh, DB-2/325, Husn Ara Manzil, Kalyani, West Bengal, India.
E-mail: prof_arkb@yahoo.co.in

Access this article online

Quick Response Code:

Website: www.ijrh.org

DOI: 10.4103/ijrh.ijrh_25_17

How to cite this article: Khuda-Bukhsh AR. An overview of research at University of Kalyani in exploring some basic issues of Homoeopathy. Indian J Res Homoeopathy 2017;11:147-57.

in regard to human genome, maintaining suitable controls. In all such experiments, we diluted the homoeopathic remedies with double distilled water in such a way that the alcohol concentration of the vehicle of the drug always was brought down to <1% to avoid any known alcohol effect on cells and the 'control' alcohol ('placebo') was also diluted to the same extent for a proper comparison of the actual drug effect.

X-ray-induced Cytogenetical Effects and their Modulations by Potentised Homoeopathic Drugs

Chromosomes house DNA, the genetic material that controls all metabolic, enzymatic and other physiological activities of all living organisms except for a few, where RNA is the genetic material. Therefore, any damage to DNA is detrimental and needs immediate action for its protection/repair. A well-established and efficient intrinsic mechanism to protect/repair DNA/chromosomes has already been known. Hence, we wanted to see if micro-doses of ultra-highly diluted homoeopathic drugs could demonstrate their ability to influence the genomic repair mechanism. X-ray exposure to animal causes quantifiable chromosome damages for each dose as manifested by aberrations of different types. We conducted controlled experimental studies for testing ability of several potentised remedies against X-ray-induced genotoxic/cytogenetical/enzymatic damages in mice *in vivo*.[1-6] It was observed that multiple cytogenetical end-points such as chromosomal aberrations, micro-nucleated erythrocytes, sperm head anomaly and mitotic indices of mice (*M. musculus*), exposed to whole-body X-irradiation in sub-lethal doses, could be favourably modulated by administration of a potentised homoeopathic drug, *Arnica montana*, commonly used against shock and injury, as compared to that of several well-maintained controls. The drug-fed X-irradiated mice clearly showed lesser amount of chromosomal damage compared to that of succussed alcohol (placebo)-fed, diluted alcohol-fed and water-fed controls. Thus, *Arnica montana* 30C appeared to show protective effect against cytogenetical damage (including repair of DNA damage) induced by whole-body X-irradiation in mice. Mice-fed *Arnica* 30C both pre- and post-irradiation showed the best protective effect, followed by only post- and pre-fed mice, in that order. Subsequently, similar works were carried out more extensively in X-irradiated mice with some other ultra-highly diluted drugs used against shock and injury, such as *Hypericum* 30C, *Ruta graveolens* 30C, *X-ray* 30C and *Ginseng* 30C and 200C, which also showed anti-radiation effects in experimental mice as compared to succussed alcohol-fed controls. Thus, the homoeopathic drugs demonstrated their ability to trigger the repair process of chromosome/DNA damage, for which the 'repair genes' must have been involved.

The 'gene regulatory hypothesis' was first presented by this author in the All India Congress of Cytology and Genetics held in 1993 at Berhampur University, Orissa, the proceedings of which was published in 1995,[7] and later, in a slightly modified form in a British Medical Journal in 1997,[8] mainly based on our findings on anti-radiation efficacy of some potentised homoeopathic drugs. Subsequently, *Arnica montana* 30C also appeared to protect sonication-induced cytogenetical damages in mice; however, when actinomycin D, a transcription blocker, was used alongside the homoeopathic drug in mice, the ameliorating effects of the homoeopathic drug were apparently absent.[9] Repair of DNA in mice is known to be regulated and performed by the concerted effort of certain genes (such as XP-A, B, C, D, E and F in mammals) and without active involvement of these repair genes, a complete repair of damaged DNA is not possible. *Arnica montana* 30C also showed its protective effect in bacteria *Escherichia coli* subjected to ultraviolet (UV)-irradiation and interestingly enough showed the expected over-expression of the concerned repair genes Uvr A, Uvr B and Uvr C in the drug-fed series; however, no such changes in expression level of the repair genes were observed in the succussed alcohol 30C fed control.[10] Similarly genes regulating entry and expulsion of arsenic in bacteria *E. coli* were also found to be favourably modulated by administration of *Arsenicum album* 30C.[11]

Testing Homoeopathy for Enzymatic Modulations

We tested efficacy of several potentised homoeopathic remedies in protecting against cytogenetic damage inflicted by some toxic chemicals on the basis of isopathic principle, treating toxicity effects of different toxic chemicals with ultra-high dilutions of the same toxic substance, as per the homeopathic doctrine 'like cures like' taking not only cytogenetical parameters but also some other scientifically accepted parameters such as enzymatic and non-enzymatic proteins and other relevant genotoxic protocols.[12-23] Cytogenetical endpoints as well as certain toxicity biomarkers such as acid phosphatase (AcP) and alkaline phosphatase (AlkP), alanine amino transferase (ALT) and aspartate amino transferase (AST), lipid peroxidation and reduced glutathione were considered. Incidentally, modulation of physiological action as manifested in protein biomarkers essentially will need change in transcription signals which are under direct control of specific genes or part of DNA.

Amelioration of Arsenic Toxicity in Mice and Human with Potentised *Arsenicum album*

Administration of a potentised homeopathic remedy, *Arsenicum album* 30C, positively modulated various parameters of toxicity in arsenic-intoxicated experimental mice vis-à-vis proper control.[12-23] Results of a pilot human trial followed by a more extensive trial involving nearly 200 people living in a few high-risk groundwater arsenic-contaminated villages revealed that *Arsenicum album* 30C and 200C could show signs of amelioration in respect of a large number of scientific protocols and toxicity biomarkers of arsenicosis, such as arsenic contents in urine and blood (nail and hair of a few), ALT, AST, AcP and AlkP, antinuclear antibody titre and haematological parameters.[24-27] Arsenic content

of urine and blood decreased significantly along with other positive ameliorative changes in 'verum'-fed subjects. Even signs/symptoms of arsenicosis were minimised or disappeared after treatment for a few months. Subsequently, a millesimal potency *Arsenicum album* 0/3 also appeared to show benefits in the recovery process from arsenicosis.[28] The toxicity biomarkers included various liver enzymes, antioxidants and stress markers, which are under regulation of specific genes. Arsenic intoxication is known to disrupt synthesis/functioning of as many as 200 enzymes, which are again under genetic control. Thus, amelioration in enzymatic activities towards normal would speak for the drug's influence on regulation of expression of numerous relevant enzyme-regulating genes. Subsequently, both *Arsenicum album* 30C and 200C were also found to ameliorate genotoxicity/clastogenicity induced by repeated injections of arsenic trioxide in mice, the latter potency showing marginally better ameliorative potential. Not only in human but also in mammalian animal model (mice), *Arsenicum album* 30C also demonstrated its ability to modulate protein biomarkers and gene expressions in the unicellular budding yeast, *Saccharomyces cerevisiae* (a member of primitive unicellular eukaryote) exposed to arsenate.[29] *Arsenicum album* 6C also protected sodium arsenite-induced apoptosis in *S. cerevisiae*.[30] Interestingly, homoeopathically prepared glucose 30C demonstrated its capability to increase glucose uptake through over-expression of permease gene and Ars A gene (enhancing ATPase activity for expulsion of arsenic) in arsenite-stressed bacteria *E. coli*, a member of the unicellular prokaryote group, while administration of *Arsenicum album* 30C induced over-expression of Ars B and C genes[31] (for arsenic tolerance and pumping out of arsenic), the placebo-treated *E. coli* failed to elicit such results. In another interesting and pioneering study, capability to modulate gene expression and to target the genes (DNA) for synthesising altered transcriptome by potentised homoeopathic drugs could also be evidenced by a novel phage (virus) bacteria infectivity experiment.[32] Thus, ultra-high dilutions of *Arsenicum album* could produce ameliorating effects in both higher and lower eukaryotes as well as in prokaryotes. These results are significant in many ways. First, *E. coli* with a very simple genetic system could respond to potentised ultra-high dilutions in a positive manner, which would mean that the homoeopathic remedies can somehow have direct influence on genetic system and many hypotheses that implicate nervous system as an essential part of the mechanism become redundant in these lower organisms. Second, the bacterium could recognise between glucose 30C and *Arsenicum album* 30C which produced differential expression of certain relevant target genes; this again would speak for its support for the gene regulatory hypothesis. Indeed, similar ameliorative results were also obtained in *S. cerevisiae* in response to arsenic insult and treatment with *Arsenicum album* 30C,[29] and here too, the succussed alcohol 30C (control) failed to elicit any positive response, thereby lending support for the 'molecular imprint' hypothesis of the homeopathic drug that makes it different in action from the chemically alike 'succussed alcohol'.

Amelioration of Thalassemia Patients on Hydroxyurea Treatment

Thalassemia is a disease essentially caused by gene mutations (haemoglobinopathy). A human trial consisting of some 38 thalassemic patients who had been on hydroxyurea treatment for varying periods of time, but their improvement having stopped or declined (as revealed from data of various blood parameters such as ferritin level, haemoglobin level and status of enlargement of spleen/liver, etc.) was undertaken to examine if supportive treatment with certain potentised homoeopathic drugs could bring improvement in their health condition, particularly in respect of some haematological parameters.[33,34] Administration of *Ceanothus*, *Pulsatilla* and *Ferrum metallicum* not only positively modulated blood picture in respect of ferritin and haemoglobin levels and decrease in size of spleen and liver of the 'verum'-fed subjects but also improved their mental state dramatically.[34] All children became more energetic and cheerful after receiving homoeopathic remedies as supportive care, speaking for the ameliorative effect of the drugs on 'mental state' of patients even with genetic deficiencies.

Homoeopathic Drugs and their Bioactive Ingredients in Cancer Cells *In vivo* and *In vitro*: Nano-formulation and Nano-precipitation

Certain homoeopathic drugs, both in low and high dilutions and in their nano-encapsulated forms, have been reported to have anticancer/anti-hepatotoxic effects by us, both in mice[35-54] and rats[55-58] *in vivo* and in various cancer cells *in vitro*.[59-91] Among these, several studies were conducted involving both *in vivo* and *in vitro* conditions that yielded similar results in both conditions, and mice proved to be an excellent mammalian animal model for conducting *in vivo* studies,[92,93] even for providing evidence for expression of repair genes after UV-irradiation,[94] or hyperglycaemia-regulatory genes.[95,96] Cancer is a multi-step multi-gene process, generally initiated by mutation and transformation of proto-oncogene to oncogene. The entire process of carcinogenesis involves a large number of metabolic changes strictly under control of certain genes; regulation of these genes goes faulty, leading to transformation of cells. The transformed cells then attain immortalisation and are characterised by uncontrolled cell division and growth, with faulty expression of certain genes including the signal transducing genes. The dividing cells subsequently attain ability to move out from its original location to invade other surrounding tissue (metastasis). Most of these cancer cells are also capable of skipping cell death signals (apoptosis). Therefore, one way of determining anti-cancer potential of a drug rests on its ability to kill cancer cells either by apoptosis or necrosis. We have provided convincing evidence of modulation of relevant signal proteins triggered by certain homeopathic drugs and their active ingredients while in all these cases, corresponding 'placebo

controls' failed to elicit such positive signal responses. Favourable modulation of expression of aryl hydrocarbon receptor (Ahr receptor) has also been demonstrated in drug-fed DMBA-induced skin cancer mice, while the placebo failed to bring about such changes.[47] Modulation of expression of genes occurred at both mRNA and protein levels so was true for expression of matrix metalloproteinases genes associated with metastasis of cancer. Results from immunofluorescence, western blot, real-time polymerase chain reaction and electron microscopic studies supported effects at both histopathological and molecular levels. We utilised accepted protocols for nano-encapsulating dried extracts of homoeopathic mother tinctures of several homoeopathic drugs such as *Gelsemium sempervirens*, *Polygala senaga* and *Peumus boldus* and thus produced actual poly (D, L-lactic-co-glycolic) acid loaded nanoparticles of these drugs in the acceptable nano-range sizes (about 100 nm or so) for drug delivery and compared their biological effects on cancer cells *in vivo* and *in vitro* with that of their respective unencapsulated mother tincture extracts and 'blank' controls.[74] We found that at a much reduced dose, the formulated nano-encapsulated medicines acted much faster and more effectively and in a target-specific manner as compared to their crude forms or mother tinctures, which can provide analogy to the action of mother tinctures versus potentised forms of a homeopathic remedy. Interestingly, nanoparticles of original drug substances have recently been reported to exist in ultra-high dilutions of homoeopathic remedies although their actual role or mode of action could not be understood. Thus, our study on deliberate nano-encapsulation of homoeopathic drugs and their bioactive ingredients and revelation of their pathways of action and signalling mechanism, distribution in different tissues and ability to cross blood–brain barriers are some significant findings which can serve as a link with the findings of nanoparticles in high dilutions of homoeopathic remedies. The nanoparticles observed in high dilutions are claimed to be produced during the dynamisation process while we consciously produced them with a scientifically accepted protocol and characterised them physicochemically with most modern techniques such as atomic force, scanning and transmission electron microscopies and dynamic light scattering and by utilising several firmly established biological protocols. Some of the bioactive ingredients isolated from mother tinctures and their nano-encapsulated forms have also been reported to have stronger anticancer effects by us subsequently. Thus, these results have implications on the homoeopathic doctrine 'more diluted, stronger the action of drugs'. Further, some of these nanoparticles had some role in changing ultra-structural orientation of water molecules carrying specific 'information bits' as suggested in the well-known 'memory of water' concept. These nanoparticles could also interact with DNA-producing conformational changes required for epigenetic modifications.[97-102] To our knowledge, this happens to be the first approach to implicate ability of potentised homoeopathic drugs to interact with genome affecting possible change in transcriptome to initiate the recovery process of a disease, which led to the discovery of some personalised homoeopathic remedies by potentising specific segments of DNA bearing some specific genes.[103,104]

Studies on Epigenetic Modifications and on Global Microarray of Genes

DNA microarrays are widely used to measure expression levels of large numbers of genes simultaneously, with the aid of selective probes under highly stringent conditions, for monitoring expression levels to study the effects of certain treatments, for example, to identify genes whose expression is changed in response to pathogens or drugs. In our recent studies,[99-102] we conducted microarray analysis in regard to modulating capability of *Hydrastis canadensis* 30C and *Condurango* 30C, two homoeopathic remedies known to have anti-cancer effects from clinical studies, against placebo control. Expression profiles of certain genes of the drug-treated HeLa cells *in vitro* were significantly different from that of the placebo-treated cells. This suggests that drugs and placebo differed in their ability to trigger gene responses, particularly those implicated in cancer.

Epigenetic modifications are the hallmarks of cancer. We demonstrated[97,99,101] that homeopathic drugs could modulate epigenetic modifications in cancer cells *in vivo* and *in vitro*. They influenced DNA methylation–demethylation and histone acetylation/deacetylation favourably for regulating gene expressions.

Concluding Remarks

Experimental results support that potentised homeopathic drugs, though devoid of any original drug molecule, were still capable of acting favourably in a multidirectional manner, by triggering a gene/set of gene(s) ('master' genes), followed by a cascade of downstream gene actions responsible for the recovery process. However, how this was precisely accomplished in higher complex organisms still needs further in-depth research. In our experiments involving both bacteria and bacteriophages containing simple genetic systems, certain genes of interest were very clearly modulated by potentised homoeopathic drugs (30C), confirming that some homeopathic remedies had anti-viral effect and could have direct influences on the genetic system.

Further studies are warranted to learn more precisely if nanoparticles of the drugs have a key role in transferring information to water/aquatic ethanol molecules presumably by their ability of modulating their sub-molecular architecture. On the basis of all evidences available, the gene regulatory hypothesis offers an acceptable logical explanation of the molecular mechanism involved in biological action of the ultra-highly diluted homeopathic remedies in all living organisms, plants and animals, possibly by triggering processes of epigenetic modifications through methylation/demethylation of DNA and acetylation/deacetylation of histone, which are an integral part of the epigenetic modification route. However,

further works are necessary to elucidate as to how the remedies may carry specific 'signals' or 'molecular imprints' of drug that can be identified by specific receptors of the cells as a trigger to turn 'on' or 'off' some relevant genes, initiating a cascade of gene actions to alter and correct the gene expressions that might have gone wrong during development and production of the pathological disorder/disease. Currently, it appears that homoeopathic medicines could manipulate the signalling mechanism in a bid to reverse/rectify signals towards initiating recovery process on the road.[47]

Regulation of gene expression is a very complex phenomenon in the higher eukaryotes such as mammals, during this process, the roles of 'activators', 'enhancers', 'gene-silencing' and phosphorylation/dephosphorylation have to be more clearly assessed to understand the actual molecular mechanisms involved in transmission of 'information' of the homeopathic remedy down to the 'execution' level for initiation and completion of disease recovery process. Each signal may be communicated to a particular gene by a separate activator (signal recognition particle). Signals are often communicated to transcriptional regulators through signal transduction pathways. However, how a homeopathic medicine diluted beyond Avogadro's limit can elicit response in a cell receptor and bind with the receptor (that is, ligand role) is not yet precisely known although we have shown in one experiment that *Secale cornutum* 30C could activate Ahr receptor which needs ligand-activation to function.[47] More precise role of nanoparticles in Homeopathy has also to be further studied although we have put in quite extensive data on record to suggest their possible role in biological action and put forward a significant step to link up the findings of nanoparticles in ultra-high dilutions of homeopathic remedies and their possible biological function, mechanism and pathways of action.

Acknowledgements

The author is indebted to his research students and collaborators for their sincere work in this challenging field, and to the funding agencies, particularly to Boiron Laboratories, Lyon, France and Ministry of AYUSH, New Delhi, who sanctioned a grant for the work. Grateful acknowledgement is also made to UGC, Government of India, for awarding Emeritus Fellowship to the author.

Financial support and sponsorship

Nil.

Conflicts of interest

None declared.

References

1. Khuda-Bukhsh AR, Goswami S, Barat A, Sadhukhan G, Mukherjee A. X-Ray Induced Chromosomal Aberrations and Their Alterations by the Oral Administration of a Homeopathic Drug, Arnica Montana, in Mice. Proceedings Seminars on the "Effects of Environmental Agents on Genetical Systems", Calcutta University; 18-20 October, 1982. p. 2-3.
2. Khuda-Bukhsh AR. Some homeopathic drugs as radio-protective agents in X-irradiated mice. In: Manna GK, Sinha U, editors. Perspective in Cytology Genetics. Vol. 5. All India Congress of Cytology & Genetics; 1986. p. 407-12.
3. Khuda-Bukhsh AR, Maity S. Alterations of cytogenetic effects by oral administration of a homeopathic drug, *Ruta Graveolens*, in mice exposed to sub-lethal X-irradiation. Berlin J Res Hom 1990;1:264-74.
4. Khuda-Bukhsh AR, Banik S. Assessment of cytogenetical damages in X-irradiated mice and their alterations by oral administrations of a potentized homeopathic drug, Ginseng 200. Berlin J Res Hom 1991;1:254-63.
5. Banik S, Khuda-Bukhsh AR. Quantitative assessment of sperm head anomaly in X-irradiated mice and the alteration of frequency by the oral administration of a potentized homeopathic drug, Ginseng. Proc. Sym. "Zoological Research in Relation to Man and Environment", Calcutta University, 1-4 March, 1992. Proc Zool Soc (Calcutta) 1992;45:243-8.
6. Banik S, Khuda-Bukhsh AR. Alterations of cytogenetical and haematological effects by ultra-low doses of Ginseng in whole-body X-irradiated mice. Nucleus. 1996;49:28-35.
7. Khuda-Bukhsh AR. Alteration of X-ray effects by homeopathic drugs: A new approach in radio-protection. In: Manna GK, Roy SC, editors. Perspectives in Cytology and Genetics. Vol. 8. Calcutta: All India Congress of Cytology and Genetics held in 1993 and Published; 1995. p. 649-63.
8. Khuda-Bukhsh AR. Potentized homeopathic drugs act through regulation of gene expression: A hypothesis to explain their mechanism and pathways of action *in vivo*. Complement Ther Med 1997;5:43-6.
9. Chakrabarti J, Biswas SJ, Khuda-Bukhsh AR. Cytogenetical effects of sonication in mice and their modulations by actinomycin D and a homeopathic drug, Arnica 30. Indian J Exp Biol 2001;39:1235-42.
10. Das S, Saha SK, De A, Das D, Khuda-Bukhsh AR. Potential of the homeopathic remedy, arnica montana 30C, to reduce DNA damage in *Escherichia coli* exposed to ultraviolet irradiation through up-regulation of nucleotide excision repair genes. Zhong Xi Yi Jie He Xue Bao 2012;10:337-46.
11. De A, Das D, Dutta S, Chakraborty D, Boujedaini N, Khuda-Bukhsh AR. Potentized homeopathic drug Arsenicum Album 30C inhibits intracellular reactive species generation and up-regulates expression of arsenic resistance gene in arsenic exposed bacteria *Escherichia coli*. Zhong Xi Yi Jie He Xue Bao 2012;10:210-27.
12. Mitra K, Kundu SN, Khuda-Bukhsh AR. Efficacy of a potentized homoeopathic drug (Arsenicum Album-30) in reducing cytotoxic effects produced by of arsenic trioxide in mice. I. On rate of accumulation of arsenic in certain vital organs. Complement Ther Med 1998;6:178-84.
13. Datta S, Mallick P, Khuda-Bukhsh AR. Efficacy of a potentized homeopathic drug (Arsenicum Album -30) in reducing genotoxic effects produced by arsenic trioxide in mice: Comparative studies of pre-, post-, pre- and post-oral administration and comparative efficacy of two microdoses. Complement Ther Med 1999;7:62-75.
14. Mitra K, Kundu SN, Khuda-Bukhsh AR. Efficacy of a potentized homoeopathic drug (Arsenicum Album-30) in reducing cytotoxic effects produced by of arsenic trioxide in mice.II. On alterations in body weight, tissue weight and total protein. Complement Ther Med 1999;7:24-34.
15. Kundu SN, Mitra K, Bukhsh AR. Efficacy of a potentized homoeopathic drug (Arsenicum-album-30) in reducing cytotoxic effects produced by arsenic trioxide in mice: III. enzymatic changes and recovery of tissue damage in liver. Complement Ther Med 2000;8:76-81.
16. Kundu SN, Mitra K, Khuda-Bukhsh AR. Efficacy of a potentized homoeopathic drug (Arsenicum Album-30) in reducing cytotoxic effects produced by of arsenic trioxide in mice. IV. On certain pathological conditions, gel electrophoretic protein profiles, DNA and RNA. Complement Ther Med 2000;8:157-65.
17. Datta SS, Mallick PP, Rahman Khuda-Bukhsh AA. Comparative efficacy of two microdoses of a potentized homoeopathic drug, Cadmium Sulphoricum, in reducing genotoxic effects produced by cadmium chloride in mice: A time course study. BMC Complement Altern Med 2001;1:9.
18. Datta S, Khuda-Bukhsh AR. Efficacy of a potentized homeopathic drug, Stannum 30, in modifying clastogenic effects of Stannum chloride in mice. Perspectives Cytol Genet 1998;9:345-51.

19. Datta S, Biswas SJ, Khuda-Bukhsh AR. Comparative efficacy of pre-feeding, post-feeding and combined pre- and post-feeding of two microdoses of a potentized homeopathic drug, mercurius solubilis, in ameliorating genotoxic effects produced by mercuric chloride in mice. Evid Based Complement Alternat Med 2004;1:291-300.
20. Mallick P, Mallick JC, Guha B, Khuda-Bukhsh AR. Ameliorating effect of microdoses of a potentized homeopathic drug, Arsenicum album, on arsenic-induced toxicity in mice. BMC Complement Altern Med 2003;3:7.
21. Khuda-Bukhsh AR. The efficacy of potentized homeopathic drug in combating arsenic poisioning: A suggestive scientific probe. Cytol Genet 2001;10:231-9.
22. Banerjee P, Bhattacharyya SS, Pathak S, Naoual B, Belon P, Khuda-Bukhsh AR, *et al.* Comparative efficacy of two microdoses of a potentized homeopathic drug, arsenicum album, to ameliorate toxicity induced by repeated sublethal injections of arsenic trioxide in mice. Pathobiology 2008;75:156-70.
23. Banerjee P, Biswas SJ, Belon P, Khuda-Bukhsh AR. A potentized homeopathic drug, Arsenicum album 200, can ameliorate genotoxicity induced by repeated injections of arsenic trioxide in mice. J Vet Med A Physiol Pathol Clin Med 2007;54:370-6.
24. Khuda-Bukhsh AR, Pathak S, Guha B, Karmakar SR, Das JK, Banerjee P, *et al.* Can homeopathic arsenic remedy combat arsenic poisoning in humans exposed to groundwater arsenic contamination? A preliminary report on first human trial. Evid Based Complement Alternat Med 2005;2:537-48.
25. Belon P, Banerjee P, Choudhury SC, Banerjee A, Biswas SJ, Karmakar SR, *et al.* Can administration of potentized homeopathic remedy, Arsenicum album, alter antinuclear antibody (ANA) titer in people living in high-risk arsenic contaminated areas? I. A correlation with certain hematological parameters. Evid Based Complement Alternat Med 2006;3:99-107.
26. Belon P, Banerjee A, Karmakar SR, Biswas SJ, Choudhury SC, Banerjee P, *et al.* Homeopathic remedy for arsenic toxicity? Evidence-based findings from a randomized placebo-controlled double blind human trial. Sci Total Environ 2007;384:141-50.
27. Belon P, Biswas SJ, Roy Karmakar S, Banerjee P, Banerjee A, Das JK, *et al*. Is an elevated antinuclear antibody titer in subjects living in groundwater arsenic contaminated villages inducative of a time-dependent effect of arsenic exposure? Environ Sci Indian J 2007;2:10-6.
28. Khuda-Bukhsh AR, Banerjee A, Biswas SJ, Karmakar SR, Banerjee P, Pathak S, *et al.* An initial report on the efficacy of a millesimal potency Arsenicum Album LM 0/3 in ameliorating arsenic toxicity in humans living in a high-risk arsenic village. Zhong Xi Yi Jie He Xue Bao 2011;9:596-604.
29. Das D, De A, Dutta S, Biswas R, Boujedaini N, Khuda-Bukhsh AR, *et al.* Potentized homeopathic drug Arsenicum Album 30C positively modulates protein biomarkers and gene expressions in *Saccharomyces cerevisae* exposed to arsenate. Zhong Xi Yi Jie He Xue Bao 2011;9:752-60.
30. Das D, De A, Khuda-Bukhsh AR. A potentized homeopathic remedy, Arsenicum Album 6C can attenuate Sodium arsenite induced apoptosis in the budding yeast *Saccharomyces cerevisiae.* Proc AICCG Bodh Gaya 2011;15:55-66.
31. Khuda-Bukhsh AR, De A, Das D, Dutta S, Boujedaini N. Analysis of the capability of ultra-highly diluted glucose to increase glucose uptake in arsenite-stressed bacteria *Escherichia coli*. Zhong Xi Yi Jie He Xue Bao 2011;9:901-12.
32. Saha SK, Das S, Khuda-Bukhsh AR. Phenotypic evidence of ultra-highly diluted homeopathic remedies to act at gene expression level: A novel probe on experimental phage infectivity in bacteria. J Chin Integr Med 2012;10:210-27.
33. Banerjee A, Chakrabarty SB, Karmakar SR, Chakrabarty A, Biswas SJ, Haque S, *et al.* Can homeopathy bring additional benefits to thalassemic patients on hydroxyurea therapy? encouraging results of a preliminary study. Evid Based Complement Alternat Med 2010;7:129-36.
34. Banerjee A, Roy Karmakar S, Paul S, Houque S, Das S, Khuda-Bukhsh AR. EFFICACY of some homeopathic drugs in modulating different blood parameters in thalassemic patients: A short-term study. Clinical and Experimental Homeopathy. 2010; 2:1:1-10. Available from: https://www.researchgate.net/publication/283460456_EFFICACY_OF_SOME_HOMEOPATHIC_DRUGS_IN_MODULATING_DIFFERENT_BLOOD_PARAMETERS_IN_THALASSEMIC_PATIENTS_A_SHORT-TERM_STUDY?_iepl%5BviewId%5D=L2ERukH3Nb4cYmv20ZkraP7Ajko0pI8HcGE4&_iepl%5Bcontexts%5D%5B0%5D=prfhpi&_iepl%5Bdata%5D%5BstandardItemCount%5D=15&_iepl%5Bdata%5D%5BuserSelectedItemCount%5D=0&_iepl%5Bdata%5D%5BtopHighlightCount%5D=2&_iepl%5Bdata%5D%5BstandardItemIndex%5D=13&_iepl%5Bdata%5D%5BstandardItem13of15%5D=1&_iepl%5BtargetEntityId%5D=PB%3A283460456&_iepl%5BinteractionType%5D=publicationPreviewImage [Last accessed on 2017 Aug 23].
35. Biswas SJ, Khuda-Bukhsh AR. Effect of a homeopathic drug, chelidonium, in amelioration of p-DAB induced hepatocarcinogenesis in mice. BMC Complement Altern Med 2002;2:4.
36. Biswas SJ, Khuda-Bukhsh AR. Evaluation of protective potentials of a potentized homeopathic drug, chelidonium majus, during azo dye induced hepatocarcinogenesis in mice. Indian J Exp Biol 2004;42:698-714.
37. Biswas SJ, Pathak S, Bhattacharjee N, Das JK, Khuda-Bukhsh AR. Efficacy of the potentized homeopathic drug, Carcinosin 200, fed alone and in combination with another drug, Chelidonium 200, in amelioration of p-dimethylaminoazobenzene-induced hepatocarcinogenesis in mice. J Altern Complement Med 2005;11:839-54.
38. Pathak S, Kumar Das J, Jyoti Biswas S, Khuda-Bukhsh AR. Protective potentials of a potentized homeopathic drug, *Lycopodium*-30, in ameliorating azo dye induced hepatocarcinogenesis in mice. Mol Cell Biochem 2006;285:121-31.
39. Pathak S, Bhattacharjee N, Das JK, Choudhury SC, Karmakar SR, Banerjee P, *et al.* Supportive evidence for the anticancerous potential of alternative medicine against hepatocarcinogenesis in mice. Forsch Komplementmed 2007;14:148-56.
40. Biswas SJ, Bhattacharjee N, Khuda-Bukhsh AR. Efficacy of a plant extract (*Chelidonium majus* L.) in combating induced hepatocarcinogenesis in mice. Food Chem Toxicol 2008;46:1474-87.
41. Bhattacharjee N, Pathak S, Khuda-Bukhsh AR. Amelioration of carcinogen-induced toxicity in mice by administration of a potentized homeopathic drug, natrum sulphuricum 200. Evid Based Complement Alternat Med 2009;6:65-75.
42. Bhattacharjee N, Banerjee P, Anisur RK. Homeopathic drugs natrum sulphuricum and Carcinosin prevent azo dye-induced hepatocarcinogenesis in mice. Indian J Biochem Biophys 2009;46:307-18.
43. Pathak S, Banerjee A, Paul S, Khuda-Bukhsh AR. Protective potentials of a plant extract (*Lycopodium clavatum*) on mice chronically fed hepato-carcinogens. Indian J Exp Biol 2009;47:602-7.
44. Karmakar SR, Biswas SJ, Khuda-Bukhsh AR. Anti-carcinogenic potentials of a plant extract (*Hydrastis canadensis*): I. Evidence from *in vivo* studies in mice (*Mus musculus*). Asian Pac J Cancer Prev 2010;11:545-51.
45. Pathak S, Banerjee A, Khuda-Bukhsh AR. Efficacy of ethanolic spore extract of *Lycopodium clavatum* in reducing induced hepatotoxicity and genotoxicity in mice. Int J Biol Chem Sci 2010;4:770-81.
46. Bhattacharyya SS, Paul S, Dutta S, Boujedaini N, Khuda-Bukhsh AR. Anti-oncogenic potentials of a plant coumarin (7-hydroxy-6-methoxy coumarin) against 7,12-dimethylbenz [a] anthracene-induced skin papilloma in mice: The possible role of several key signal proteins. Zhong Xi Yi Jie He Xue Bao 2010;8:645-54.
47. Khuda-Bukhsh AR, Bhattacharyya SS, Paul S, Dutta S, Boujedaini N, Belon P, *et al.* Modulation of signal proteins: A plausible mechanism to explain how a potentized drug secale cor 30C diluted beyond Avogadro's limit combats skin papilloma in mice. Evid Based Complement Alternat Med 2011;2011:286320.
48. Paul S, Bhattacharyya SS, Samaddar A, Boujedaini N, Khuda-Bukhsh AR. Further evidences of anti-cancer potentials of root extract of *Polygala senega* against benzo[a] pyrene induced lung cancer in mice. J Chin Integr Med 2011;9:320-7.
49. Bhattacharjee N, Khuda-Bukhsh AR. Two homeopathic remedies used intermittently provide additional protective effects against

hepatotoxicity induced by carcinogens in mice. J Acupunct Meridian Stud 2012;5:166-75.
50. Das S, Das J, Samadder A, Paul A, Khuda-Bukhsh AR. Efficacy of PLGA-loaded apigenin nanoparticles in Benzo[a]pyrene and ultraviolet-B induced skin cancer of mice: Mitochondria mediated apoptotic signalling cascades. Food Chem Toxicol 2013;62:670-80.
51. Paul A, Das J, Das S, Samadder A, Khuda-Bukhsh AR. PLGA nano-encapsulation of chelidonine enhances the ameliorative potential against cadmium induced oxidative damage and hepatic injury in mice. Environ Toxicol Pharmacol 2013;36:937-47.
52. Das S, Das J, Samadder A, Paul A, Khuda-Bukhsh AR. Efficacy of PLGA-loaded apigenin nanoparticles in Benzo[a]pyrene and ultraviolet-B induced skin cancer of mice: Mitochondria mediated apoptotic signalling cascades. Food Chem Toxicol 2013. pii: S0278-6915(13) 00675-3.
53. Sikdar S, Mukherjee A, Ghosh S, Khuda-Bukhsh AR. Condurango glycoside-rich components stimulate DNA damage-induced cell cycle arrest and ROS-mediated caspase-3 dependent apoptosis through inhibition of cell-proliferation in lung cancer, *in vitro* and *in vivo*. Environ Toxicol Pharmacol 2014;37:300-14.
54. Ghosh S, Sikdar S, Mukherjee A, Khuda-Bukhsh AR. Evaluation of chemopreventive potentials of ethanolic extract of *Ruta graveolens* against A375 skin melanoma cells *in vitro* and induced skin cancer in mice *in vivo*. J Integr Med 2015;13:34-44.
55. Banerjee A, Pathak S, Biswas SJ, Roy-Karmakar S, Boujedaini N, Belon P, *et al. Chelidonium majus* 30C and 200C in induced hepato-toxicity in rats. Homeopathy 2010;99:167-76.
56. Sikdar S, Mukherjee A, Bishayee K, Paul A, Saha S, Ghosh S, *et al*. Assessment of apoptotic and anticancer potentials of a potentized homeopathic drug, Condurango 30C, in Benzo[a]pyrene-induced lung cancer of rat: The signalling cascade. J Pharmacopuncture 2013;16:11-22.
57. Sikdar S, Khuda-Bukhsh AR. Post-cancer treatment of Condurango 30C, traditionally used in homeopathy, ameliorates tissue damage and stimulates reactive oxygen species in benzo[a]pyrene-induced lung cancer of rat. Humanitas Tradit Med 2013;3:e25. Available from: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.923.6923&rep=rep1&type=pdf; http://www.e-tang.org/journal.do?method=viewFullTextArchive&journalSeq=J000027&menuId=0202&introMenuId=0202. [Last accessed on 2017 Aug 11].
58. Sikdar S, Mukherjee A, Khuda-Bukhsh AR. Ethanolic extract of *Marsdenia condurango* ameliorates Benzo[a]pyrene-induced lung cancer of rats: Condurango ameliorates baP-induced lung cancer in rats. J Pharmacopuncture 2014;17:7-17.
59. Bhattacharyya SS, Mandal SK, Biswas R, Paul S, Pathak S, Boujedaini N, *et al. In vitro* studies demonstrate anticancer activity of an alkaloid of the plant *Gelsemium sempervirens*. Exp Biol Med (Maywood) 2008;233:1591-601.
60. Bhattacharyya SS, Paul S, Khuda-Bukhsh AR. Encapsulated plant extract (*Gelsemium sempervirens*) poly (lactide-co-glycolide) nanoparticles enhance cellular uptake and increase bioactivity *in vitro*. Exp Biol Med (Maywood) 2010;235:678-88.
61. Mandal SK, Biswas R, Bhattacharyya SS, Paul S, Dutta S, Pathak S, *et al.* Lycopodine from *Lycopodium clavatum* extract inhibits proliferation of HeLa cells through induction of apoptosis via caspase-3 activation. Eur J Pharmacol 2010;626:115-22.
62. Khuda-Bukhsh AR, Bhattacharyya SS, Paul S, Boujedaini N. Polymeric nanoparticle encapsulation of a naturally occurring plant scopoletin and its effects on human melanoma cell A375. Zhong Xi Yi Jie He Xue Bao 2010;8:853-62.
63. Biswas R, Mandal SK, Dutta S, Bhattacharyya SS, Boujedaini N, Khuda-Bukhsh AR, *et al.* Thujone-rich fraction of thuja occidentalis demonstrates major anti-cancer potentials: Evidences from *in vitro* studies on A375 cells. Evid Based Complement Alternat Med 2011;2011:568148.
64. Paul S, Bhattacharyya SS, Boujedaini N, Khuda-Bukhsh AR. Anticancer potentials of root extract of *Polygala senega* and its PLGA nanoparticles-encapsulated form. Evid Based Complement Alternat Med 2011;2011. pii: 517204.
65. Paul A, Bishayee K, Ghosh S, Mukherjee A, Sikdar S, Chakraborty D, *et al.* Chelidonine isolated from ethanolic extract of *Chelidonium majus* promotes apoptosis in HeLa cells through p38-p53 and PI3K/AKT signalling pathways. Zhong Xi Yi Jie He Xue Bao 2012;10:1025-38.
66. Bishayee K, Mukherjee A, Paul A, Khuda-Bukhsh AR. Homeopathic mother tincture of Conium initiates reactive oxygen species mediated DNA damage and makes HeLa cells prone to apoptosis. TANG Int J Genuine Tradit Med 2012;2:e-26.
67. Samadder A, Das S, Das J, Paul A, Boujedaini N, Khuda-Bukhsh AR, *et al.* The potentized homeopathic drug, *Lycopodium clavatum* (5C and 15C) has anti-cancer effect on hela cells *in vitro*. J Acupunct Meridian Stud 2013;6:180-7.
68. Das S, Das J, Samadder A, Paul A, Khuda-Bukhsh AR. Strategic formulation of apigenin-loaded PLGA nanoparticles for intracellular trafficking, DNA targeting and improved therapeutic effects in skin melanoma *in vitro*. Toxicol Lett 2013;223:124-38.
69. Das S, Das J, Samadder A, Khuda-Bukhsh AR. Dihydroxy-isosteviol methyl ester from *Pulsatilla nigricans* induces apoptosis in HeLa cells: Its cytoxicity and interaction with calf thymus DNA. Phytother Res 2013;27:664-71.
70. Paul A, Das S, Das J, Samadder A, Bishayee K, Sadhukhan R, *et al.* Diarylheptanoid-myricanone isolated from ethanolic extract of *Myrica cerifera* shows anticancer effects on HeLa and PC3 cell lines: Signalling pathway and drug-DNA interaction. J Integr Med 2013;11:405-15.
71. Ghosh S, Bishayee K, Paul A, Mukherjee A, Sikdar S, Chakraborty D, *et al.* Homeopathic mother tincture of *Phytolacca decandra* induces apoptosis in skin melanoma cells by activating caspase-mediated signaling via reactive oxygen species elevation. J Integr Med 2013;11:116-24.
72. Ghosh S, Bishayee K, Khuda-Bukhsh AR. Graveoline isolated from ethanolic extract of *Ruta graveolens* triggers apoptosis and autophagy in skin melanoma cells: A novel apoptosis-independent autophagic signaling pathway. Phytother Res 2014;28:1153-62.
73. Mukherjee A, Boujedaini N, Khuda-Bukhsh AR. Homeopathic Thuja 30C ameliorates benzo(a)pyrene-induced DNA damage, stress and viability of perfused lung cells of mice *in vitro*. J Integr Med 2013;11:397-404.
74. Das S, Das J, Samadder A, Bhattacharyya SS, Das D, Khuda-Bukhsh AR, *et al.* Biosynthesized silver nanoparticles by ethanolic extracts of *Phytolacca decandra*, *Gelsemium sempervirens*, *Hydrastis canadensis* and *Thuja occidentalis* induce differential cytotoxicity through G2/M arrest in A375 cells. Colloids Surf B Biointerfaces 2013;101:325-36.
75. Bhattacharyya SS, Das J, Das S, Samadder A, Das D, De A, *et al.* Rapid green synthesis of silver nanoparticles from silver nitrate by a homeopathic mother tincture *Phytolacca decandra*. Zhong Xi Yi Jie He Xue Bao 2012;10:546-54.
76. Ghosh S, Bishayee K, Paul A, Mukherjee A, Sikdar S, Chakraborty D, *et al.* Homeopathic mother tincture of *Phytolacca decandra* induces apoptosis in skin melanoma cells by activating caspase-mediated signaling via reactive oxygen species elevation. J Integr Med 2013;11:116-24.
77. Chakraborty D, Ghosh S, Bishayee K, Mukherjee A, Sikdar S, Khuda-Bukhsh AR, *et al.* Antihyperglycemic drug *Gymnema sylvestre* also shows anticancer potentials in human melanoma A375 cells via reactive oxygen species generation and mitochondria-dependent caspase pathway. Integr Cancer Ther 2013;12:433-41.
78. Bishayee K, Chakraborty D, Ghosh S, Boujedaini N, Khuda-Bukhsh AR. Lycopodine triggers apoptosis by modulating 5-lipoxygenase, and depolarizing mitochondrial membrane potential in androgen sensitive and refractory prostate cancer cells without modulating p53 activity: Signaling cascade and drug-DNA interaction. Eur J Pharmacol 2013;698:110-21.
79. Bishayee K, Paul A, Ghosh S, Sikdar S, Mukherjee A, Biswas R, *et al.* Condurango-glycoside-A fraction of *Gonolobus condurango* induces DNA damage associated senescence and apoptosis via ROS-dependent p53 signalling pathway in HeLa cells. Mol Cell Biochem 2013;382:173-83.
80. Paul A, Das S, Das J, Samadder A, Khuda-Bukhsh AR. Cytotoxicity and apoptotic signalling cascade induced by chelidonine-loaded PLGA nanoparticles in HepG2 cells *in vitro* and bioavailability of nano-chelidonine in mice *in vivo*. Toxicol Lett 2013;222:10-22.

81. Saha SK, Sikdar S, Mukherjee A, Bhadra K, Boujedaini N, Khuda-Bukhsh AR, *et al.* Ethanolic extract of the Goldenseal, *Hydrastis canadensis*, has demonstrable chemopreventive effects on HeLa cells *in vitro*: Drug-DNA interaction with calf thymus DNA as target. Environ Toxicol Pharmacol 2013;36:202-14.
82. Sikdar S, Kumar Saha S, Rahman Khuda-Bukhsh A. Relative apoptosis-inducing potential of homeopa-thic condurango 6C and 30C in H460 lung cancer cells *in vitro*: Apoptosis-induction by homeopathic condurango in H460 cells. J Pharmacopuncture 2014;17:59-69.
83. Mukherjee A, Sikdar S, Bishayee K, Boujedaini N, Khuda-Bukhsh AR. Flavonol isolated from ethanolic leaf extract of *Thuja occidentalis* arrests the cell cycle at G2-M and induces ROS-independent apoptosis in A549 cells, targeting nuclear DNA. Cell Prolif 2014;47:56-71.
84. Mondal J, Panigrahi AK, Khuda-Bukhsh AR. Anticancer potential of *Conium maculatum* extract against cancer cells *in vitro*: Drug-DNA interaction and its ability to induce apoptosis through ROS generation. Pharmacogn Mag 2014;10:S524-33.
85. Mondal J, Samadder A, Khuda-Bukhsh AR. Psorinum 6 × triggers apoptosis signals in human lung cancer cells. J Integr Med 2016;14:143-53.
86. Mondal J, Das J, Shah R, Khuda-Bukhsh AR. A homeopathic nosode, Hepatitis C 30 demonstrates anticancer effect against liver cancer cells *in vitro* by modulating telomerase and topoisomerase II activities as also by promoting apoptosis via intrinsic mitochondrial pathway. J Integr Med 2016;14:209-18.
87. Das J, Das S, Samadder A, Bhadra K, Khuda-Bukhsh AR. Poly (lactide-co-glycolide) encapsulated extract of *Phytolacca decandra* demonstrates better intervention against induced lung adenocarcinoma in mice and on A549 cells. Eur J Pharm Sci 2012;47:313-24.
88. Paul A, Das J, Das S, Samadder A, Khuda-Bukhsh AR. Anticancer potential of myricanone, a major bioactive component of *Myrica cerifera*: Novel signaling cascade for accomplishing apoptosis. J Acupunct Meridian Stud 2013;6:188-98.
89. Mondal J, Bishayee K, Panigrahi AK, Khuda-Bukhsh AR. Low doses of ethanolic extract of boldo (*Peumus boldus*) can ameliorate toxicity generated by cisplatin in normal liver cells of mice *in vivo* and in WRL-68 cells *in vitro*, but not in cancer cells *in vivo* or *in vitro*. J Integr Med 2014;12:425-38.
90. Mondal J, Panigrahi AK, Khuda-Bukhsh AR. Poly(lactic-co-gycolic acid)-loaded boldine nanoparticles alleviates cisplatin induced hepatotoxicity in normal liver cells *in vitro* via DNA targeting: Drug-DNA interaction. Int J Ther Appl 2015;29:24-31.
91. Mondal J, Panigrahi AK, Khuda-Bukhsh AR. Physico-chemical and ultra-structural characterizations of PLGA-loaded nanoparticles of Boldine and their efficacy in ameliorating cisplatin induced hepatotoxicity in normal liver cells *in vitro*. J Innov Pharmaceuticals Biol Sci 2015;2:506-21.
92. Khuda-Bukhsh AR. Mice as a model for homeopathy research. Homeopathy 2009;98:267-79.
93. Samadder A, Das J, Das S, Das D, De A, Bhadra K, *et al.* Dihydroxy-isosteviol methyl ester of *Pulsatilla nigricans* extract reduces arsenic-induced DNA damage in testis cells of male mice: Its toxicity, drug-DNA interaction and signaling cascades. Zhong Xi Yi Jie He Xue Bao 2012;10:1433-42.
94. Das S, Das J, Paul A, Samadder A, Khuda-Bukhsh AR. Apigenin, a bioactive flavonoid from *Lycopodium clavatum*, stimulates nucleotide excision repair genes to protect skin keratinocytes from ultraviolet B-induced reactive oxygen species and DNA damage. J Acupunct Meridian Stud 2013;6:252-62.
95. Samadder A, Chakraborty D, De A, Bhattacharyya SS, Bhadra K, Khuda-Bukhsh AR, *et al.* Possible signaling cascades involved in attenuation of alloxan-induced oxidative stress and hyperglycemia in mice by ethanolic extract of *Syzygium jambolanum*: Drug-DNA interaction with calf thymus DNA as target. Eur J Pharm Sci 2011;44:207-17.
96. Chakraborty D, Samadder A, Dutta S, Khuda-Bukhsh AR. Antihyperglycemic potentials of a threatened plant, *Helonias dioica*: Antioxidative stress responses and the signaling cascade. Exp Biol Med (Maywood) 2012;237:64-76.
97. Bishayee K, Sikdar S, Khuda-Bukhsh AR. Ultra-highly diluted gonolobus condurango extract inhibits histone de-Acetylase2 activity in cervix cancer cells *in vitro*: Evidence of epigenetic modification in cell cycle arrest. J Pharmacopunctue 2013;16:7-13.
98. Saha SK, Khuda-Bukhsh AR. Berberine alters epigenetic modifications, disrupts microtubule network, and modulates HPV-18 E6-E7 oncoproteins by targeting p53 in cervical cancer cell HeLa: A mechanistic study including molecular docking. Eur J Pharmacol 2014;744:132-46.
99. Sikdar S, Khuda-Bukhsh AR. Condurango 30C induces epigenetic modification of lung cancer specific tumour suppressor genes via demethylation. Forsch Komplementarmed/Res Complement Med 2015;22:172-9.
100. Khuda-Bukhsh AR. Current trends in ultra-high dilution research with particular reference to gene regulatory hypothesis: Review article. Nucleus 2014;57:3-17.
101. Saha SK, Roy S, Khuda-Bukhsh AR. Ultra-highly diluted plant extracts of *Hydrastis canadensis* and *Marsdenia condurango* induce epigenetic modifications and alter gene expression profiles in HeLa cells *in vitro*. J Integr Med 2015;13:400-11.
102. Saha SK, Roy S, Khuda-Bukhsh AR. Evidence in support of gene regulatory hypothesis: Gene expression profiling manifests homeopathy effect as more than placebo. Int J High Dilution Res 2013;12:162-7.
103. Kay PH, Khuda-Bukhsh AR. The contribution of homeogenomic and homeogenetic studies to the support of the practice of homeopathy. Indian J Res Homeopath 2016;10:1010107. [DOI: 10.4103/0974-7168.183858]. Available from: http://www.ijrh.org. [Last Accessed on: 2017 Aug 09], IP: 106.203.182.198].
104. Kay PH, Khuda-Bukhsh AR. An introduction to homeogenomic considerations in innovation of high dilution technology. Homeopathy in Practice. Alliance of Registered Homeopaths (ARH), 2016. p. 46-52.

कल्याणी विश्वविद्यालय में होम्योपैथी के कुछ मौलिक मामलों की खोज पर अनुसंधान का एक अवलोकन

सार

वर्तमान समय में होम्योपैथी का सामना कुछ प्रमुख मुद्दों से हो रहा है जैसे– (क) कैसे होम्योपैथिक औषधि के औषधीय गुण माध्यम में हस्तांतरित होते है और कैसे माध्यम द्वारा इन गुणों को प्रतिधारित किया जाता है। (ख) अल्ट्रा–हाइली डाईल्युटेड रेमेडीज (उपचार) में किसी भी मूल औषधीय पदार्थ की अनुपस्थिति में, यह जैविक प्रणालियों में कैसे कार्य कर सकता है और (ग) जैविक क्रियाओं की क्रिया विधि और मार्ग की वैज्ञानिक व्याख्या की कमी, जिसमें 'समः समम्: शमयति' और 'मन–शरीर संवाद' जैसे रहस्य शामिल हैं। हमने जीवित स्तनधारी मॉडल चूहों में पूरे शरीर के एक्स–विकिरण द्वारा प्रदत्त साइटोजेनेटिक नुकसान की रक्षा/ठीक करने में अल्ट्रा–हाइली डाईल्युटेड होम्योपैथिक औषधियों की क्षमता का नियंत्रित अध्ययन के माध्यम से प्रदर्शन किया। हमने आर्सेनिक, कैडमियम, मरक्युरी (पारा) और स्टेनलम से प्रभावित चूहों में साइटोजेनेटिक नुकसान की जांच की तथा कई वैज्ञानिक प्रोटोकॉल का उपयोग कर उनसे संबंधित साल्ट से उत्तेजित अल्ट्रा–हाइडाईल्युसंस से प्राप्त होम्योपैथिक औषधियों द्वारा उनका उपचार किया। आर्सेनिक–दूषित भूजल से पीड़ित लोगों के विरुद्ध आर्सेनिकम एल्बम की प्रभावकारिता पर एक मानव परीक्षण किया व मनुष्यों में थैलेसीमिया और चूहों में कैंसर में कुछ होम्योपैथिक उपचारों की प्रभावकारिता का परीक्षण किया। हमने होम्योपैथिक मदर टिंचर्स और उनके जैव सक्रिय (बायोएक्टिव) घटकों से नैनो कैप्सूल का निर्माण किया और सिल्वर नाइट्रेट से होम्योपैथिक मदर टिंचर्स द्वारा सिल्वर की नैनो–प्रेसीपिटेशन को प्रेरित किया और उन्हें उनके भौतिक गुणों और जैविक क्रियाओं के लिए चित्रित किया। हमने नैनो कणों के ऊतक वितरण, सटीक तंत्र और उनकी क्रिया के मार्गों का अध्ययन किया है जिसमें इनविवो और इनविट्रो, दोनों में कुछ संकेत (सिग्नल) प्रोटीनों और उनके मार्ग शामिल हैं। इस दृष्टिकोण ने 'जल की स्मृति' और तंत्र को उत्प्रेरित करने में औषध नैनो कणों की भूमिका तथा एपीजिनेटिक संशोधनों के माध्यम से होम्योपैथिक उपचार की कार्रवाई के मार्ग जो हमारे 'जीन नियामक परिकल्पना' का समर्थन करते हैं, को स्पष्ट करने में महत्वपूर्ण योगदान दिया।

Ein Überblick über die Forschung an der Universität von Kalyani bei der Erforschung einige grundlegende Fragen der Homöopathie

Abstrakt

Die Homöopathie wird mit bestimmten wichtigen Hauptfragen konfrontiert: i) Wie wird die arzneiliche Eigenschaft des homöopathischen Mittels auf das Vehikel übertragen und aufgenommen; ii) wie kann eine hochgradig verdünnte Arznei ohne ursprüngliche Arzneimittelsubstanz in einem biologischen Systemen wirken; und iii) ehlende wissen-schaftliche Erklärung des biologischen Wirkungsmechanismus, einschließlich der Myster-ien von "Ähnliches wird durch Ähnliches geheilt" und "Körper-Psyche-Interaktion".

Wir haben mittels kontrollierter Untersuchungen das Potenzial hochgradig verdünnter homöopathischer Arzneien zum Schutz/Reparatur von zytogenetischen Schäden, hervorgerufen durch eine Ganzkörper-Röntgenbestrahlung im Säugetier-Mäuse-Modell in vivo gezeigt. Wir untersuchten zytogenetische Schäden bei Mäusen, die mit Arsen, Cadmi-um, Quecksilber und Zinn vergiftet worden sind, und deren Sanierung durch homöopa-thische Arzneimittel, die aus verschüttelten ultra-hohen Verdünnungen ihres jeweiligen Salzes gewonnen worden sind und bei vielen wissenschaftlichen Untersuchungen eing-esetzt wurden. Wir haben eine Studie zur Wirksamkeit von Arsenicum album an Menschen, die von arsenhaltigem Grundwasser verseuchten worden sind, durchgeführt. Wir testeten die Wirksamkeit einiger homöopathischer Mittel bei Krebserkrankungen von Mäusen und Thalassämie beim Menschen. Wir produzierten Nano-Kapseln homöopathischer Urtinkturen und deren bioaktiven Komponenten, induzierten die Nano-Präzipitation von Silber aus Silbernitrat durch homöopathische Urtinkturen und charakterisierten ihre physikalisch-chemischen Eigenschaften sowie ihre biologische Wirkung. Wir untersuchten die Verteilung von Nanopartikeln, deren präzisen Mechanismus und ihre Wirkungsweise, die bestimmte Signalproteine und deren Wirkungsweise involvierten, sowohl in vivo als auch in vitro. Dieser Ansatz hat einen bedeutenden Beitrag zur Aufklärung der Rolle von arzneilichen Nanopartikeln bei der Induktion von "Gedächtnis des Wassers" und dem Mechanismus und der Wirkungsweise homöopathischer Arzneimittel über epigenetische Modifikationen, die unsere "Genregulationshypothese" unterstützt haben, geleistet.

Una visión general de la investigación en la Universidad de Kalyani en la exploración algunas cuestiones básicas de la homeopatía

Resumen

La homeopatía se ha visto confrontada a determinados planteamientos importantes: i) ¿de qué forma se transmiten las propiedades medicinales del medicamento al vehículo y cómo puede éste retenerlas?; ii) en ausencia de cualquier sustancia farmacológica original en las ultradiluciones de los medicamentos, ¿cómo es posible que siga actuando en los sistemas biológicos? y iii) la falta de elucidación científica del mecanismo y de las vías de la acción biológica, incluyendo los misterios de "lo similar puede curar lo similar" y de la "interacción mente-cuerpo". A través de estudios controlados, hemos demostrado la capacidad de los medicamentos homeopáticos a altas diluciones de ofrecer una protección / reparación de las lesiones citogenéticas que la radiación corporal total provoca en el modelo mamífero de ratonesin vivo. Hemos examinado las lesiones citogenéticas en ratones intoxicados con arsénico, cadmio, mercurio y estaño, y su resolución con medicamentos homeopáticos derivados de las ultradilucionessucusionadas de la correspondientes sal, aplicando muchos protocolos científicos. Hemos realizado un ensayo humano sobre la eficacia de *Arsenicumalbumen* víctimas contaminadas por arsénico a través de las aguas freáticas. Hemos investigado la eficacia de algunos medicamentos homeopáticos en el cáncer de ratones y en la talasemia del ser humano. Hemos confeccionado nanocápsulas de tinturas madre homeopáticas y sus componentes bioactivos, y hemos inducido la nanoprecipitación de la plata a partir del nitrato de plata mediante tinturas madre homeopáticas que después se caracterizaron en cuanto a sus propiedades físico químicas y a su acción biológica. Hemos estudiado la distribución de las nanopartículas, el mecanismo preciso y las vías que implican determinadas proteínas de señalización y sus vías, tanto *in vivo*como*in vitro*. Este enfoque ha proporcionado datos significativospara elucidar el papel de las nanopartículasmedicamentosasen inducir la "memoria del agua", así como el mecanismo y las vías de acción de los medicamentos homeopáticos a través de modificaciones epigenéticas que apoyan nuestra "hipótesis de regulación genética".

Un aperçu de la recherche à l'Université de Kalyani en explorant Quelques problèmes fondamentaux de l'homéopathie

Résumé

L'homéopathie a été confrontée à certaines questions majeures telles que (i) comment la propriété médicale du médicament homéopathique est-elle transférée au véhicule et retenue par celui-ci ; (ii) en l'absence de toute substance médicamenteuse originale dans des remèdes ultra-dilués, comment peut-elle agir dans les systèmes biologiques et (iii) le manque d'élucidation scientifique du mécanisme et des voies de l'action biologique, y compris les mystères tels que « les semblables se guérissent par les semblables » et 'l'interaction esprit-corps'. Par le biais des études contrôlées, nous avons démontré la capacité des médicaments homéopathiques ultra-dilués à protéger/réparer les dommages cytogénétiques infligés par l'irradiation-X du corps entier chez les souris modèles mammaliennes in vivo. Nous avons examiné les dommages cytogénétiques chez les souris intoxiquées par l'arsenic, le cadmium, le mercure et l'étain et leur remédiation à l'aide des médicaments homéopathiques dérivés de dilutions agitées ultra-élevées de leur sel respectif, en déployant de nombreux protocoles scientifiques. Nous avons effectué un essai humain sur l'efficacité d'Arsenicum Album chez les victimes contaminées par l'arsenic des eaux souterraines. Nous avons testé l'efficacité de certains remèdes homéopathiques dans le cas du cancer chez les souris et de la thalassémie chez l'homme. Nous avons produit des nano-capsules de teintures-mères homéopathiques et de leurs composants bioactifs et avons induit une nano-précipitation de l'argent à partir du nitrate d'argent par des teintures-mères homéopathiques et les avons caractérisées selon leurs propriétés physico-chimiques et leur action biologique. Nous avons étudié à la fois in vivo et in vitro la distribution tissulaire des nanoparticules, les mécanismes précis et les voies de leur action qui impliquaient certaines protéines de signalisation et leurs voies. Cette approche a apporté une contribution significative à l'élucidation du rôle des nanoparticules médicamenteuses dans l'induction de 'la mémoire de l'eau', le mécanisme et les voies d'action des remèdes homéopathiques à travers les modifications épigénétiques qui ont soutenu notre 'hypothèse de régulation des gènes'.

卡利亞尼大學探索研究概況 順勢療法的一些基本問題

摘要

順勢療法要面對一些重大問題： i) 順勢療法藥物藥用特性如何透過載體轉移或保留；ii) 極度稀釋療劑沒有任何原來的藥物物質，它是如何在生物系統中起作用；iii) 缺乏生物作用機制和途徑的科學解釋，包括「相似者能治癒」和「身心相互作用」的奧秘。通過對照研究，我們証明在小鼠體內動物模型內，極度稀釋的順勢療法藥物可以對全身照射X光所造成的細胞遺傳學損傷有保護／修復的作用。我們研究了白砷、鎘、汞和錫中毒白鼠的細胞遺傳學損傷，以及服用了順勢療法藥物（即由其相應礦物鹽加能的極度稀釋療劑）後的修復作用，當中使用了許多科學性的研究方案。我們就白砷對飲用受白砷污染地下水受害者的療效之影響進行了人體試驗。我們測試了一些順勢療法療劑在治療患癌老鼠和人類地中海貧血的療效。我們生產了順勢療法母酊以及他們的生物活性成份的納米膠囊，亦通過順勢療法母酊的方式，由硝酸银誘導銀的納米沉澱，得出其物理化學和生物作用的性質。我們研究了納米顆粒的組織分佈、其精確的機制和它們作用的途徑，它們的作用涉及某些信號蛋白及其途徑，包括體內和體外。這種方法對闡明藥物納米粒子在「水記憶」中的角色作出了重大的貢獻，而且支持了我們「基因調控假設」的表觀遺傳學，有助闡明順勢療法療劑的機制和途徑。