INTRODUCTION AND LITERATURE REVIEW
Introduction and Literature Review

Despite occasional challenges faced by homeopathy, it still continues to have the support of millions of people around the world because of

i) Its efficacy to remove disease (clinical) symptoms

ii) Use in ultra-low doses without any known side-effects

iii) Its affordability and availability

iv) Its ability to cure even chronic cases, and finally

v) Its applicability to patients who may show allergic reaction to some life-saving orthodox medicines and/or are scared to undergo surgery

But nevertheless the sustained campaign against homeopathy paved the way for the initiation of research to explore the possibility of proving the efficacy of the diluted potentized ultra-low doses of homeopathic remedies in an acceptable scientific approach

One line of approach was to perform double-blind placebo-controlled trials to combat the skeptics' contention that patients claimed to have recovered through administration of homeopathic remedies would have actually done so, even though they would not have received any medicine whatsoever

But there are so many intricacies to resolve beyond establishing the efficacy of homeopathic remedies. One pertinent question to be asked would be to explain to prove by scientific experimentations how the alcoholic vehicles of the homeopathic remedies could be "charged" or "energized" with the medicinal properties of a specific remedy. In other words, one has to explain
in terms of physico-chemical properties of the vehicle which would render them the ability not only to receive the medical properties but also make them able to retain them for a long time. Not only that, one has also to find an answer to how the medicinal properties transferred to aquatic alcohol can also be efficiently transferred to the globules which can also store them for later use.

The next area of concern is to understand and clarify the events by which micro-doses of the ultra-high diluted remedies could arouse biological responses and activate healing processes bringing the patients back to recovery.

Quite understandably then, homeopathy is a subject much complex than apparently it looks like to be. Therefore, research into any of these aspects could call for expertise encompassing several branches of science namely physics, chemistry, biology, physiology and medicine.

Since many case reports dealing with positive recovery enacted by homeopathic remedies were mostly reported in obscure homeopathic medical journals (most of which are not peer-reviewed for scientific approach or reliability), many earlier reports are put to question. However, results of many scientifically conducted clinical trials undoubtedly point to the efficacy of some potentized homeopathic remedies in removing disease symptoms.

Certain technological problems and difficulties make homeopathic research rather complicated in nature. Homeopathic doctrine believes in a holistic approach in dealing with various symptoms of the diseases and adopts a principle of individualization of cases. One example can make it clear. There is no fixed medicine for any particular disease in homeopathy, but there are particular medicines for particular sets of symptoms. The individualized
disease symptoms rather than the disease itself are primary in the selection of the specific drug. Furthermore, in the selection of a homeopathic remedy "mind" and general constitution are also given due importance particularly in cases of chronic diseases. Therefore, the remedy may be different not only for the same disease but also for persons suffering from the same disease who differ in some specific symptoms. In fact, a particular medicine is to be selected critically based on totality of symptoms. For example, three patients with influenza may differ in two symptoms in the following manner:

Patient I is very restless and frequently wants to take a little water. Patient II is not restless, prefers to stay quiet and wants to take a large amount of water less frequently and Patient III is not restless, lies in bed semiconscious, does not like to talk with anybody and has no thirst. Rhus toxicodendron (or Arsenicum album) is the most suitable remedy for patient I, Bryonia alba for patient II, and Gelsemium gnitidum (or Gelsemium sempervirens) for patient III. Another influenza patient with a high temperature and a red face and throbbing headache may require yet another remedy, Belladona. A clinical trial on influenza patients to determine the efficacy of any particular remedy, say Rhus toxicodendron or Gelsemium may not find that all influenza patients respond equally well [Khuda-Bukhsh 2006]. Thus the first difficulty in carrying out scientific clinical trials (Randomized clinical trial) [Fernstein 1980] is the problem of selecting one among several drugs for the same disease, which may not actually be the most suitable drug for all. Because there is not a single specific treatment for a single disease, the conventional form of clinical trials would demand for sets of symptoms and corresponding remedies used in homeopathy in order to show causal efficacy for all of them [Walach 1998]. Thus to find out whether a homeopathic approach is comparable or superior to a standard treatment in general for all sorts of patients, a rather cumbersome randomized comparison study would be called for [Khuda-Bukhsh 2006]. The question to be answered by a double-blind
randomized control trial with placebo (i.e., the vehicle of the drug) is whether the homeopathic remedies as such are superior in efficacy to placebo. Another important aspect in human trial is ethical issue. Ethical issues in administering placebo to ailing people with chronic or serious diseases also need due consideration [Khuda-Bukhsh et al. 2005]. Therefore, it can be rather difficult to establish the causal efficacy of homeopathic remedies above placebo because of such considerations necessitating meta-analysis of controlled clinical trial to arrive at a conclusion of either positive clinical effects of a drug over placebo on human subjects with any given disease (i.e., similar set of symptoms) or no such effect. Therefore, one way of knowing how far homeopathic remedies are efficacious will be to accumulate data on several meta-analyses published so far in some cited journals. To have a fair idea on several attempts made so far by some prominent workers are given below.

Table-1. A Few Prominent Clinical Trials on Homeopathy Published from 1998 to 2002 (cited from NCCAM, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20892 USA, updated March 2006, Web nccam.nih.gov)

<table>
<thead>
<tr>
<th>Citation</th>
<th>Description</th>
<th>Findings</th>
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<tr>
<td>Vickers and Smith, 2002</td>
<td>Seven trials were included in the review (three prevention and four treatment trials), only two studies had sufficient information for complete data extraction</td>
<td>The homeopathic remedy oscillococcinum appears safe and effective in reducing the duration of influenza, but has no effect on prevention</td>
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<tr>
<td>Study</td>
<td>Design Description</td>
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<td>Lewith et al., 2002</td>
<td>Randomized, double-blinded, placebo-controlled trial of 242 participants aged 18 to 55 years</td>
<td>Trial compared an oral homeopathic treatment to placebo in asthmatic people allergic to house dust. Authors found the homeopathic treatment &quot;no better than placebo.&quot; They noted &quot;some differences between the homeopathic immunotherapy and placebo for which we have no explanation.&quot;</td>
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<td>Oberbaum et al., 2001</td>
<td>Randomized, double-blinded, placebo-controlled trial in 32 children, 30 completed the study</td>
<td>Traumeel S, a homeopathic skin cream, may significantly reduce the severity and length of pain and inflammation of the tissues lining the inside of the mouth from chemotherapy in children being treated with bone marrow transplantation.</td>
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| Taylor et al., 2000           | Randomized, double-blinded, placebo-controlled trial of 51 participants aged 17 years or older (50 completed the study) | Team tested the hypothesis that homeopathy is a placebo by examining effects of an oral homeopathic preparation in patients with perennial allergic rhinitis. They found a "significant objective improvement in nasal airflow" compared with the placebo group. However, both groups reported subjective improvement in "nasal symptoms" (with no statistically
<table>
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<th>Study</th>
<th>Design and Details</th>
<th>Findings</th>
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<td>Jacobs et al, 2000</td>
<td>Randomized, double-blind, placebo-controlled trial of 126 children, 116 completed the study</td>
<td>Individualized homeopathic treatments improved digestive problems in children with acute childhood diarrhea. Results are consistent with findings of a previous study.</td>
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<tr>
<td>Weiser et al, 1999</td>
<td>Randomized, double-blind trial of 146 people</td>
<td>For the treatment of hay fever, a homeopathic nasal spray is as efficient and well tolerated as a conventional therapy, Cromolyn sodium.</td>
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<td>Rastogi et al, 1999</td>
<td>Randomized, double-blind, placebo-controlled trial of 100 people between 18 and 50 (71 percent male/29 percent female)</td>
<td>A subgroup of patients with HIV in the symptomatic phase, receiving treatment, had increased levels of CD4 cells at the end of the trial, the placebo subgroup did not.</td>
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<td>Vickers et al, 1998</td>
<td>Randomized, double-blind, placebo-controlled trial of 519 people, 400 completed the study</td>
<td>Homeopathic remedies, including arnica, are not effective for muscle soreness following long-distance running.</td>
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Authors concluded that the objective evidence supports that "homeopathic dilutions differ from placebo."
The homeopathic treatment vertigoheel, and the standard treatment of betahistine, are equally effective in reducing the frequency, duration, and intensity of vertigo attacks.

Table-2. Systematic Reviews and Meta-Analyses of Clinical Trials of Homeopathy (cited from NCCAM, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20892 USA, updated March 2006, Web nccam.nih.gov)

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<td>Weiser et al, 1998</td>
<td>Randomized, double-blinded, controlled trial of 119 people, 105 completed the study</td>
<td>Author found that the reviews failed to provide strong evidence in favor of homeopathy. No homeopathic remedy was proven by convincing evidence to yield clinical effects that are different from placebo or from other control intervention for any medical condition. Positive recommendations for use of homeopathy in clinical practice are not supported, and &quot;homeopathy cannot be viewed as an evidence-based form of therapy&quot; until more convincing results are available.</td>
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<tr>
<td>Study</td>
<td>Methodological Analysis</td>
<td>Conclusion/Recommendation</td>
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<td>Linde et al., 2001</td>
<td>Analyzed the methodological quality of 207 randomized trials collected for 5 previously published reviews on homeopathy, two herbal medicines (St John's wort and echinacea), and acupuncture</td>
<td>Authors found that the majority of trials had major weaknesses in methodology and/or reporting. Homeopathy trials were &quot;fewer frequently randomized and reported less details than the other types.</td>
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<td>Cucherat et al., 2000</td>
<td>Analyzed 16 randomized, controlled trials (17 comparisons were made) comparing homeopathic treatment to placebo. Work was part of a report prepared for the European Union on the effectiveness of homeopathy.</td>
<td>Authors found that the &quot;strength of evidence remains low&quot; because of trial flaws and other limitations. They added, &quot;at least one [of the tested homeopathic treatments] shows an added effect relative to placebo.&quot; Group recommended that homeopathy be studied further using the same methods used to study conventional medicine.</td>
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<td>Ernst and Pittler, 1998</td>
<td>Systematic review of eight trials</td>
<td>Rigorous clinical trials indicate arnica is not more effective than a placebo, most trials studied use of arnica for tissue trauma.</td>
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<td>Linde et al., 1997</td>
<td>Analyzed 89 trials. Each trial was controlled, compared homeopathy to a placebo, was either randomized or double-</td>
<td>Authors concluded that their results were not compatible with a hypothesis that the clinical effects of homeopathy are completely due to placebo. However, they found</td>
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insufficient evidence that homeopathy is clearly efficacious for any single clinical condition. They stated that further research is warranted if it is rigorous and systematic.

**Table 3. Systematic Reviews of Clinical Trials** (cited from NCCAM, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20892 USA, updated March 2006, Web nccam.nih.gov)

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<tr>
<td>Long and Ernst, 2001</td>
<td>Systematic review of four osteoarthritis clinical trials</td>
<td>Research on homeopathic treatment for osteoarthritis is insufficient to reliably assess the clinical effectiveness of homeopathic treatment of osteoarthritis</td>
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</table>
Controlled clinical trials indicate that homeopathic remedies appear to work better than a placebo in studies of rheumatic syndromes, but there are too few studies to draw definitive conclusions, and efficacy results are mixed.

Most of the meta-analyses would indicate the efficacy of homeopathic remedies in ameliorating or curing various disease symptoms. In view of positive action of homeopathic remedies, the pertinent question would now be asked: What is the mechanism of transfer of medicinal properties to the vehicles? A few physical concepts based on research are how available in this context, of which a few prominent ones are mentioned below. A clathrate model based on dielectric and differential scanning colorimetric measurement has been proposed by Anagnostatos et al. [1998] to explain how medicinal properties can be transferred to vehicles and possible physico-chemical differences between homeopathic dilutions and the corresponding solvent can be predicted. Some clathrates can exist even if their core molecules are removed or exchanged for solvent molecules. Since clathrates may behave like crystals, they may replicate themselves during the homeopathic dilution.
process in a similar way to crystal growth. Allegre et al. [1989] suggested that the observed oscillation of the effectiveness of homeopathic solutions at different points in the serial dilution process might be similar to the oscillatory nature of crystal growth.

Andersson et al. [1997] has been able to create individual clusters using sudden evaporative cooling. These water clusters of several thousand water molecules were found to survive high collision velocities and thereby would suggest that these clusters were extremely stable. Interestingly, alcohol also form clusters with water. Wisnewski et al. [2001] Although Jongma et al. [1998] confirmed the existence of stable molecule clusters in water using technologies involving surface impact, Yui [2000] using mass spectrometry claims some mutual destruction of clusters' ion but not neutral clusters. In fact, the presence of alcohol which can form its very own clusters may actually be favorable to the moderation of succussion energy (by increasing vapor pressure), which means that succussion is not inherently destructive but on balance may create water clusters that represent the remedy.

The leading current proposal for the mode of action of potentized homeopathic remedies is that water is capable of storing information relating to substance with which it has previously been in contact and subsequently transmits this information to pre-sensitized bio-systems. This process is believed to be mediated by structural modifications of water, analogous to the storage of information by magnetic media. Such information is retained in physical rather than chemical form. Bellavite and Signorini [2002] Studies on molecular clustering in water solutions showed that as a solution is made more and more dilute, larger, very stable aggregates developed. Samal and Geckeler [2001] This means that residual molecular clusters of original substance might be present in homeopathic dilutions.
On the other hand Suslick [1989] proposed a cavitation model to explain the necessity of succussion in energy transfer or transfer of medicinal property to the aqueous alcoholic vehicle. According to this hypothesis, succussion is responsible for imploding cavitation water vapor bubble and suggests that both the heat and the jet’s kinetic energy contribute to a unique chemical environment in the liquid. However, mechanical cavitation or succussion can also generate plasma (a gas-like state where molecules can be disrupted and or ionic state) conditions, which usually tend to destroy molecules. However, the plasma constituents can also be formed into different molecular arrangements particularly on liquid or solid surfaces. Another hypothesis tried to explain the action of homeopathic drugs like that of solitons. A soliton is a self-replicating solitary wave caused by a delicate balance between nonlinear and dispersive effects in the medium. Davydov [1994] postulated a "soliton excitation model" for homeopathic drug action. Solitons are responsible for high temperature superconductivity as well as for the well-known extra ordinary sensitivity of biological systems.

Because of ultra-high dilutions, skeptics of homeopathy claim that there is nothing in the medicines because there are no molecules or very few molecules left in the highly diluted solutions. Elia and Niccoli [1999], however, published their observations which would strongly suggest that there may indeed be "something" active in homeopathic medicines. The authors measured the amount of heat emanating from plain double distilled water and compared that with double distilled water in which a substance was mixed. Both the control water and the treated water underwent consecutive dilutions between 1 and 30 times with vigorous shaking between each dilution, representing the common pharmacological method by which homeopathic medicines are made. The authors conducted more than 500 experiments, approximately half made with double distilled water that was mixed with a specific acid (Vinegar) and base substance (NaCl) and half in the
control group of only double distilled water. They found that 92% of the test solution with the added acid or base substance had higher than expected heat emanating from them. The authors claimed that their results would strongly support the hypothesis of the existence of a memory of water advocated earlier by Davenas et al. [1988] in their controversial article on basophil degranulation which was, however, supported by a repeat trial conducted by Belon et al. [1999, 2004]. Lo [1996] also found that substances that were sequentially diluted in double distilled water at least 6 times and then vigorously shaken in between would create water clusters or ice crystals \((I_e)\) which maintained an electrical field and did not melt in room temperature water.

Anick [1998] has proposed a concept of a liquid structure involving zwitterion (charged) water clusters, which could carry medicinal information. Jongma et al. [1998] also identified the existence of neutrally charged (unprotonated) water cluster ions. Incidentally structural difference between nuclear magnetic resonance spectra or Fourier transformed infrared spectra (FTIR) of homeopathic potencies and their solvent ethanol had also been demonstrated [Weingartner 1990; Sukul et al. 2005]. Rey [2003] produced evidence that ultra-dilutions can also contain initial properties of original salts that can alter chemical and biological properties. He demonstrated that despite the ultra-high dilutions beyond Avogadro’s limit, the emitted light from ultra-dilutions of Lithium chloride and NaCl was specific to original salt dissolved initially. Thus some physical properties like thermoluminiscense of the initial substance can be retained even after the dilution of the substance beyond Avogadro’s number. However, the contention that digital signal recorded on a computer disc can produce specific biological signals could not be confirmed in a replication trial [Jonas et al. 2006].
The physico-chemical structure of the vehicle that is water and alcohol is therefore important in understanding both the mechanism of transfer of medicinal property and its subsequent retention. However, the use of glucose pellet soaked with the liquid medicine would also need explanation as to how the medicinal property could also be transferred and retained by the sugar globules.

Recently Sukul et al. [2005] tried to explain this by making FTIR spectra analysis of Potassium bromide powder soaked with a few potencies of several homeopathic remedies and showed that these powders could retain their spectral absorption properties, thereby implying that sugar globules could in the same way preserve therapeutic properties of the homeopathic remedies. However, recently Moffet et al. [2006] severely criticized this contention. Obviously more research is necessary to find a more scientific explanation as to how medicinal property can be transferred to and retained by sugar globules.

The next question to be asked is concerning the ability of the micro-doses of the ultra-high dilutions to evoke biological responses in a way that could activate or deactivate relevant biological activities capable of bringing in recovery to the patient. Several studies have been performed to address this issue of which a few prominent works will be mentioned. Studies on crystal induced inflammation as well as insulin receptor activation by oxy-anions have been conducted to understand how the hydrate structure of certain types of silica or some anesthetic agents could activate specific types of cell surface protein directly or indirectly attributable to their coincidental complementary structures [Matsumoto 1994, 1995]. On the other hand research conducted by several others has tested the biological effects of I$_E$ crystals and has found remarkable effects. Lo and Bonavida [1998] made some interesting observations when they tested a sample of such crystals on blood and found a 2-200 fold increase in cytokines (mediators of immune function that protect against infection and tumor growth). This paved the way for...
initiation of other important signal transduction studies [Jonas et al 2006, Thangapazham et al 2006a, 2006b]

Another approach of study to enlighten the possible mechanism of biological action was made by Weigant and Wijk and their group working in the University of Utrecht, the Netherland According to these researchers [Wiegant et al 1997, Van Wijk and Wiegant 1994, 1997, 1998] the stimulation of a disturbed self recovery by the application of similia principle is considered to be the essence of homeopathy Interestingly these authors studied mechanism of hormesis (meaning excitation by an impulse), which is used to describe a stimulatory effect of sub-inhibitory concentration of any toxic substance on an organism and reported altered levels of RNA for heat-shock protein produced by micro-doses treatment used per the similia principle

Aguejouf et al [1998] demonstrated thromoembolic complication to persist for several days after a single dose administration of homeopathically potentized aspirin in Wister rats subjected to experimental thrombosis induced by the laser beams Subsequently Aguejouf et al [2000] also demonstrated a potent anti-thromboembolic effect of potentized acetylsalicylic acid in similarly induced experimental thrombosis Similarly Brack et al [2003] reported effects of ultra-high dilutions of 3, 5-dichlorophenol on the luminescence of the bacteria Vibrio fischeri Some researchers have also tried to perform some experiments in the field of allergology to explore the mechanism of action of the ultra-high dilutions Boiron et al [1983] reported that homeopathic Apis and Histamine had significant effects on reducing the release of certain allergy causing chemicals from basophils, which demonstrated a possible reason for homeopathy's positive effects on allergies Recently immunological implications of homeopathic remedies on both animals and human have been splendidly
reviewed by Bellavite et al [2005, 2006a, 2006b, 2006c, 2006d] The reviews would give the reader a glimpse of all aspects of immunological studies attempted so far on homeopathy

Although most of the studies mentioned above were conducted on *in vitro* systems or cell free system, many studies have also been conducted *in vivo* mammalian models, like mice, rats, cats or cattle Many of these experiments apparently support the positive efficacy of homeopathic remedies in protection from radiation [Khuda-Bukhsh & Maity 1990, Banik and Khuda-Bukhsh 1991, 1996, Khuda-Bukhsh and Banik 1991], toxic chemicals [Mitra et al 1998, 1999, Datta et al 1999a, 1999b, Kundu et al 2000a, 2000b, Datta et al 2001, 2004, Mallick et al 2003], or carcinogens [Choudhury 1980, Biswas and Khuda-Bukhsh 2002, 2004, Biswas et al 2005, Pathak et al 2006, 2007] or in human cancer [Pathak et al 2003, Jonas et al 2006] A few of these studies included various state-of-the-art techniques including scanning and transmission electron microscopies and gene expression studies [Khuda-Bukhsh 2006, Jonas et al 2006] Incidentally most of these studies indicated that the homeopathic remedies were capable of modulating gene expressions and if transcription blockers were used along with the chemical, physical mutagens [Datta et al 1999b, Chakraborti et al 2001], the efficacy of the homeopathic drug was effectively reduced, indicating active transcription as a precondition for homeopathic action

The literature review made above would indicate that some homeopathic remedies positively influenced or ameliorated various types of cancer Cancer is a dreadful disease, most of which are incurable after they attain a certain stage (metastasis) In orthodox system of treatment, if cancerous tissues are detected at initial stage of development, these can be successfully removed surgically or can be effectively subjected to early chemotherapy or radiotherapy In these cases, there are chances of some success But in the
majority of cases the detection and confirmation of cancer at early stage is
difficult or when they are positively detected often the patients are in
considerably advanced stage, precluding successful orthodox treatment.
Further, there are severe side-effects and sufferings reported in some patients
subjected to these therapies. Therefore, supportive CAM therapies are being
advocated by many recent workers along with the orthodox treatment to give
patients a better quality of life [Balzarini et al. 2000, Richardson and Strauss
et al. 2006] But unfortunately many people or doctors lack confidence for
using homeopathy, particularly higher dilutions because of lack of scientific
validation of their efficacy, although clinical observations by many physicians
would vouch for their ameliorative effects in cancer. Homeopathy takes into
consideration totality of symptoms in a patient and depending on symptoms
various remedies like Chelidonium majus, Lycopodium clavatum, Carduus
marianus, Hydrastis canadensis, Myrica cerifera etc are used. Apart from
these remedies which are derived from plant extracts, some inter-current
remedies like Carcinosin or Cholesterinum are used. These are derived from
cancer tissues by homeopathic dilutions and are called “nosodes” [Kent 1962,
Boericke 1976, Lokie 1989] They have been reported to be of additional value
in the treatment of cancer. In the present study, therefore, the efficacy of
Hydrastis Canadensis used alone and in combination with either of these two
nosodes has been evaluated in \textit{in vivo} mouse model. Earlier studies on
Hydrastis Canadensis commonly known as Goldenseal (Family
Ranunculaceae) have been done which revealed various berberine and
protoberberine alkaloids [The National Toxicology Programme, 2007] In fact,
in Hydrastis Canadensis three major alkaloids, namely, “canadine”, which
stimulates uterine muscles, “hydrastine” and “berberine”, which are known
to have anti-spasmodic and anti-bacterial activities are of major importance in
rendering various biological activities. Of these, berberine induces cell cycle arrest and apoptosis in human gastric carcinoma SNU-5 cell line [Lin et al. 2006].

These authors [Lin et al. 2006] reported that berberine induced p53 expression and laid to the decrease of mitochondrial membrane potential, Cytochrome-c release and activation of Caspase-3 for the induction of apoptosis. Goldenseal extracts are traditionally used by native Americans to treat digestive complaints, common cold, influenza, menstrual disorders and travelers’ diarrhea as well as muscular pain [Borchers et al. 2000, Mahady and Chadwick 2001]. Hydrastine and berberine have also been reported to enable bile to flow freely from the gall bladder. Hydrastis Canadensis has also been reported to have action against liver tumors and liver malfunction [Mc Leod 2001]. Further berberine extracts have been reported to inhibit various bacterial and protozoan growths [Scaggocchio et al. 2001]. In fact hydrastine and its derivatives have been tested extensively for its various mechanisms of biological actions [Ye et al. 1989, Huang and Johnston 1990, Kim et al. 2001]. Further, berberine extracts and salts have demonstrated growth inhibition of Giardia lamblia, Entamoeba histolytica, Trychomonas vaginals [Kaneda et al. 1991] and Leishmania donovani [Ghosh et al. 1985], crude extracts are more effective than berberine salts [Kaneda et al. 1990]. Chemical properties and anti-inflammatory properties of berberine have also been highlighted by Birdsall and Kelly [1997]. Cytochrom p450 inhibition by Goldenseal extract has also been reported [Chatterjee and Franklin 2003]. However, in homeopathy both mother tincture and potentized Hydrastis have been claimed to have action against various ailments particularly related to liver disorder [Kent 1962, Boericke 1976]. Thus there has been extensive use of Hydrastis extracts as a popular herbal medicine, not only in homeopathy, but also in other systems like Ayurved, Unam, etc. So far as we are aware no systematic studies had
earlier been conducted on the efficacy of the homeopathic mother tincture or the potentized form against azo-dye induced hepatocarcinogenesis in mice. The azo-dye, N, N-dimethyl-4-(phenylazo)-benzenamine, commonly known as p-dimethylaminoazobenzene (p-DAB) has been used by chronic feeding to mice for initiating liver tumor. Carcinogenic effect of p-DAB on liver of mice and rats has been reported by several authors [Nesnow et al. 1987, Biswas and Khuda-Bukhsh 2005, Pathak and Khuda-Bukhsh 2007]. Generally large doses of p-DAB (50-250 mg/kg BW) in rats cause hepatic degeneration within 24 hours followed by local degeneration of some parenchymal cells around portal spaces (IARC 1975).

5-ethyl-5-phenyl-2, 4, 6-(IH, 3H, 5H) pyrimidinetione, widely known as Phenobarbital (PB), is also of carcinogenic potential [IARC 2001] to human, mice and rat when administrated orally [Kitagawa and Sugano 1977; Kitagawa et al. 1978, 1979, 1984; Gold et al. 1979; White et al. 1979; Uchida and Hirono 1979, 1981; Peraino 1980; Pitot et al. 1987; Maekawa et al. 1992; Lee 2000; Kinoshita et al. 2003]. PB is reported to produce hepatocellular adenoma and carcinoma when fed in combination with p-DAB in mice consistently for 60 days and more [Biswas et al. 2004]. The individual effects of chronic feeding of PB [Biswas et al. 2004] p-DAB [Biswas and Khuda-Bukhsh 2005] and combined feeding of PB and p-DAB [Biswas and Khuda-Bukhsh 2004; Pathak et al. 2006, 2007] have been extensively studied and their role in development of hepatic carcinoma was confirmed.

In the present study, therefore attempts were made to evaluate the antitumorigenic, anti-clastogenic and anti-genotoxic effects of Hydrastis Canadensis in mice (Mus musculus) taking into consideration several widely accepted cytogenetical and biochemical (toxicity bio-makers) protocols.