CHAPTER TWO

Review of Literature

2.1. Antibacterial Activity

The science dealing with the study of the prevention and treatment of diseases caused by micro-organisms is known as medical microbiology. Its sub-disciplines are virology (study of viruses), bacteriology (study of bacteria), mycology (study of fungi), phycology (study of algae) and protozoology (study of protozoa). For the treatment of diseases inhibitory chemicals employed to kill micro-organisms or prevent their growth, are called antimicrobial agents. These are classified according to their application and spectrum of activity, as germicides that kill micro-organisms, whereas micro-biostatic agents inhibit the growth of pathogens and enable the leucocytes and other defense mechanism of the host to cope up with static invaders. The germicides may exhibit selective toxicity depending on their spectrum of activity. They may act as viricides (killing viruses), bacteriocides (killing bacteria), algicides (killing algae) or fungicides (killing fungi).

The beginning of modern chemotherapy has largely been due to the efforts of Dr. Paul Ehrlich (1910), who used salvarsan, as arsenic derivative effective against syphilis. Paul Ehrlich used the term chemotherapy for curing the infectious
disease without injury to the host’s tissue, known as chemotherapeutic agents such as antibacterial, antiprotosoal, antiviral, antineoplastic, antitubercular and antifungal agents. Later on, Domagk (1953) prepared an important chemotherapeutic agent sulfanilamide.

2.2. **Classification of Antibacterial Agents**

The antibacterial agents are classified in three categories:

I. Antibiotics and chemically synthesized chemotherapeutic agents.

II. Non-antibiotic chemotherapeutic agents (Disinfectants, antiseptics and preservatives)

III. Immunological products.

2.3. **Mode Of Action**

Antimicrobial drugs interfere chemically with the synthesis of function of vital components of microorganisms. The cellular structure and functions of eukaryotic cells of the human body. These differences provide us with selective toxicity of chemotherapeutic agents against bacteria.

Antimicrobial drugs may either kill microorganisms outright or simply prevent their growth. There are various ways in which these agents exhibit their antimicrobial activity. They may inhibit
(1) Cell-wall synthesis

(2) Protein synthesis

(3) Nucleic acid synthesis

(4) Enzymatic activity

(5) Folate metabolism or

(6) Damage cytoplasmic membrane

2.4 Bacteriostatic drugs

“Homoeopathic drug having action similar to the pathogenic effect of microorganism”\(^1\) like Arsenic Album, Pyrogen, Thuja, Carbo-Animalis, Echinasia, Heparsulp, Merc Core., Nitric Acid, Phos.Acid, Phos, Pulsatilla, Anti-Crud, Silica, Sulphar and last Bapticia.

2.4.1. Arsenic Album:-

The therapeutic effects of homoeopathic Arsenicum album potencies were investigated \textit{in-vitro}, using a continuous cell line (MT4), pre-intoxicated with arsenic trioxide (As2O3), and then treated with succussed and unsuccussed
homoeopathic potencies, 6CH, 30CH and 200CH. This study aimed to verify the homoeopathic law of similars and to determine whether potencies diluted beyond Avogadro’s constant had physiological effects on cells; whether various potencies would cause different effects as suggested by the concept of hormesis; whether succussed and unsuccussed homoeopathic potencies had different effects on the cells; and to establish whether a biotechnological method could be used to evaluate the above. As2O3 was used to pre-intoxicate and the MTT assay was used to measure the percentage cytotoxicity and half maximal inhibitory concentration (IC50) of the cells. The homoeopathic potencies of Arsenicum album (6CH, 30CH and 200CH) were prepared by either succussing or allowing to diffuse for 30 s. After pre-intoxication of the MT4 cells with the IC50 As2O3 and treatment with succussed and unsuccussed Arsenicum album (6CH-200CH), the cell viability increased with increasing potency from 81% to 194% (over 72 h). The treatments and the times of exposure were found to be statistically significant determinants of cell viability, whereas succussion did not cause any significant variation in the results. The study provided evidence that a biotechnological method (namely cell viability) may be used to scientifically evaluate the physiological effects of homoeopathic potencies on human cells; it confirmed that the homoeopathic
potencies did have therapeutic effects; and that succussion was not required in the potentization method in order to produce a curative remedy\textsuperscript{(14)}

\subsection*{2.4.2. Thuja}

In the present study, leaves of Thuja orientalis were powdered and extracted by soxhlet extractor in two solvent systems that is, (E1) ethyl acetate: chloroform: ethanol (40: 30: 30) and (E2) methanol: distilled water (70:30). This study conferred the screening of phytochemical constituents, antioxidant activity and antibacterial activity of crude E1 and E2 extract and its fractions. Antioxidant activity was carried out by 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. The results indicate that E2 extract (70\% methanolic extract) had the highest antioxidant effect (85.25\% inhibition) at 100 µg/ml concentration and the crude extracts (E1 and E2 extract) showed significant (P ≤ 0.05) inhibitory activity against both gram positive and gram negative organisms. It was active against Staphylococcus aureus, Bacillus subtilis, Escherichia coli, and Agrobacterium tumefaciens. The minimum inhibitory concentrations (MICs) of E1 extract ranged from 0.40 to 0.85 mg/ml and E2 extract 0.55 to 1.15 mg/ml. The highest antibacterial potentiality was exhibited by E2 extract. The fractions also exhibited antimicrobial activity against all the selected microorganisms. The study revealed
that T. orientalis is a promising phytomedicine for antioxidant and antibacterial activity.

2.4.3. Echinacea Purpurea

Antimicrobial activities of Echinacea purpurea L. (Asteraceae) extracts obtained by classical and ultrasound solvent extraction were compared. The dry aerial part of plant was extracted by 70% ethanol at a solid-to-liquid ratio of 1:10 (m/v) and 25°C. The extract obtained by classical solvent extraction contained 29% larger amounts of phenolic compounds and 20% higher content of flavonoids. 2,2-diphenyl-1-picril hydrazyl radical (DPPH) scavenging reached 93.6% and the values of EC50 were (34.16±0.65) µg·ml$^{-1}$ and (65.48±1.12) µg·ml$^{-1}$ for the extracts obtained by the classical and ultrasound extractions, respectively. The extracts, independent of the extraction technique applied, showed a considerable growth inhibition on Candida albicans and Saccharomyces cerevisiae, while no growth inhibition zones were observed for Aspergillus niger. The diameters of inhibition zone observed for all the microorganisms were larger for extracts obtained by classical extraction than those by ultrasound extraction$^{(15)}$. 
2.4.4. Hepar Sulphuris Calcareum

Sphere of action on skin, Mucous Membrane <nerves, Connective Tissue, Respiratory, flexures, glands kidneys etc..

Suits especially scrofulous and lymphatic constitutions that are inclined to have erthropions and glandular swelling,

Unhealthy skin

Blonds with sluggish character and weak muscles

Great sensitiveness to all impression.

Locally it has specua affinity to the respiratory mucous membrane, producing croupous catarrhal inflammation, profuses secretion also easy perspiration

Infected sinus with pus forming

The tendency to suppuration is most marked and has been strong guiding symptoms in practice

The lesion spread by the formation of small papules around the side of the old lesion
Stichies in the throat extending to the ear on swallowing

Quinsy with impending suppuration

2.4.5 Nitric Acid

It is a very useful remedy in fevers. The thirstlessness during all stages has often called attention to it. Cold hands and feet. Chronic intermittent in cachectic constitutions, copious night sweats. extreme weakness, with the characteristic odor of the urine, and bleeding from some part a dark blood, this remedy will act well.

2.4.6 Phosphoricum Acidum

The homeopathic remedy Phosphoric Acid (Phos. Ac.) is prepared by diluting phosphoric acid, a common mineral acid, and it is used to cure a number of health conditions, especially given to people who are basically indifferent and lethargic.

In addition to its medicinal use, phosphoric acid has extensive industrial utilities. Phosphoric acid is used to manufacture detergents and fertilizers and it is also important in refining sugar and providing a fruity and acidic essence to soft drinks. Long back, phosphoric acid was used in conventional medicine to promote digestion. In the present times, it is used to diminish the intensity of calcium in
the blood of individuals who have developed cancerous or benign tumors in their parathyroid glands, which are found in the neck.

As a homeopathic remedy, phosphoric acid is known to have extensive uses. Although the medication is prepared by diluting phosphoric acid heavily so that the end result does not contain even the slightest trace of the mineral acid, the potency offered by the homeopathic remedy phos. ac. vis-à-vis healing is genuinely intense.

2.4.7. Phosphorus

We found that an additive for a resin, which was comprised of collagen and aluminum (Al), showed a strong and stable antibacterial effect against various bacterium under certain conditions. We tried to clarify its mechanism of action, and investigated optimum conditions for its effects. This additive (Al cross-linked collagen powder: Al-COL) absorbed phosphorus in LB medium, gradually released aluminum in the phosphorus-reduced LB medium, and exhibited a bactericidal effect. Allophane was very suitable as the control subject, because it did not release Al in the medium, decreased phosphorus levels in the medium, and the phosphorus decrease led to a reduction in bacterial growth, though not to a bactericidal effect. On the other hand, the addition of Al to the phosphorus-reduced solution led to a bactericidal effect. These results suggested that Al can exert a
strong antibacterial effect in the absence of phosphorus. This phenomenon was confirmed using film-shaped test items mixed with Al-COL powder. Furthermore, the reduction of phosphorus also synergistically led to the enhancement of the antibacterial effect of silver (Ag). The phosphorous absorption promoted the antibacterial action of Al and Ag, and Al, which has seldom been used as an antimicrobial agent, is available as an antibacterial agent in the absence of phosphorus.\(^{(17)}\)

2.4.8. Pulsatilla:

The essential oil obtained by hydrodistillation of the aerial flowering parts of Pulsatilla albana (Stev.) Bercht. & Presl. was analyzed by GC and GC/MS. Twenty-five compounds representing 97.5% of oil were identified, among them pulegone (39.1%), piperitenone (17.2%), menthone (16.1%), 1, 8-cineole (8.9%) and p-mentha-3,8-diene (4.2%). In this essential oil oxygenated monoterpenes (87.9%) predominated over monoterpenic hydrocarbons (8.3%) and sesquiterpenes (1.3%). Nonterpene hydrocarbons were not found among the identified components. Antibacterial screening of the oil showed moderate activity against certain strains of Gram-positive and Gram-negative bacteria\(^{(18)}\).
2.4.9. Anti Crud

Warts are small growths on the skin caused by a viral infection in the skin's top layer. They can happen anywhere on the body, but usually appear on the hands and feet. Warts are usually harmless and painless, but they can be disfiguring and embarrassing, and occasionally they hurt or itch. Warts may become painful if they're located in areas of repeated friction or pressure. The following are different types of warts:

- **Common warts**: usually on the hands, but can appear anywhere

- **Flat warts**: generally found on the face and back of the hands (they are smaller and smoother than other warts)

- **Genital warts**: found on the external genitalia, in the pubic area, and in the area between the thighs, but can appear inside the vagina and in the anal canal

- **Plantar warts**: found on the soles of the feet

2.4.10. Sulphur :-

Antimicrobial resistance continues to be an inexorable threat for the biomedical and biochemical researchers. Despite the novel discoveries in drug designing and
delivery, high-throughput screening and surveillance data render the prospects for new antimicrobial agents as bleak as ever. The advent of nanotechnology, however, strengthens pharmacology by offering effective therapeutics to treat this aforementioned problem. Several nanoparticles of the known elements have already been reported for their antimicrobial efficacy. Nanosized fabrication of elemental sulphur with suitable surface modifications offers to retrieve the use of sulphur (man's oldest known ecofriendly microbicide) as a potential antimicrobial agent. Sulphur nanoparticles (SNPs) are effective against both conventionally sulphur-resistant and sulphur-susceptible microbes (fungi and bacteria). Moreover, biocompatible polymers present on the surface of SNPs minimize toxicity during application. Here, we focus on various aspects of physicochemical features of SNPs and their biochemical interactions with microbes. The present review also illustrates the effects of SNPs on plants and animals in terms of cytotoxicity and biocompatibility.

2.4.11. Baptisia tinctoria

The purpose of this study was to determine the antimicrobial effect of Baptisia tinctoria extract (1:10) in 62% ethanol and Baptisia tinctoria extract (1:10) in distilled water on the in vitro growth inhibition of Staphylococcus aureus,
Staphylococcus epidermidis, Pseudomonas aeruginosa, Escherichia coli and Enterococcus faecalis respectively as compared to ethanol and distilled water control\(^{(20)}\)

2.4.12. Pyrogenium:

Pyrogenium is a Nosode and is prepared from the pus of septic abscess. It corresponds to streptococcus and other anti febrile vaccine. Pyrogenium can very conveniently be calling HOMEOPATHIC DYNAMIC ANTI SEPTIC. The pus from the septic abscess, when potentise, serves a great anti septic remedy.\(^7\)

Dr. Drysdale was the first to introduce Pyrogenium into homeopathy way back in 1880. Pyrogenium was prepared by mixing beef with water and allowing the mixture to remain as it is for around three weeks. This mixture was filtered to leaving behind a clear amber hued liquid known as sepsin. Subsequently, sepsin was blended with glycerine and was called Pyrogenium. Dr. Drysdale wrapped up by saying that when Pyrogenium is administered in a large dosage, it results in changes in t
The blood and tissues similar to those of blood poisoning following any lesion. On the contrary, smaller dosages of Pyrogenium facilitated complete recovery from problems related to the blood.\[12\]

Several evidences as well as majority of the clinical trials have been acquired from this medical preparation. However, later on, Dr. Swan had rendered latent power (potentized) a number of septic pus - a preparation that has also been proved as well as applied clinically. Interestingly, there does not appear to be any distinct difference between the effects of these two dissimilar preparations.\[12\]

It has been established that the homeopathic medicine Pyrogenium is a wonderful cure of all septic conditions that are accompanied by extreme restlessness. It has also been proved that Pyrogenium is an amazing and dynamic homeopathic antimicrobial in treating septic fevers, particularly puerperal or conditions related to childbirth. This homeopathic medicine may be extremely useful and effective in treating conditions, such as hectic typhoid; typhus (also known as typhus fever); diphtheria (a contagious ailment caused by the bacillus Corynebacterium diphtheria and distinguished by the development of a false membrane in the air passages, especially the throat); ptomaine poisoning (food poisoning believed to be caused by ptomaine); poisoning by sewer gas; dissecting
wounds, incessant malaria and aftermath of any miscarriage. All these conditions and associated symptoms call for the administration of the homeopathic medicine Pyrogenium. All types of bodily discharges by people suffering from such conditions are dreadfully unpleasant. Such bodily discharges may include vomiting, diarrhea, menstrual bleeding, lochial discharges (fluid discharges after childbirth) and even breathing. Such people experience extreme pain and violent burning sensation when they have abscesses. They may also have constant complaints that may be as old as the septic conditions themselves. In addition, such patients may also be faced with the hazards of heart failure in zymotic (a condition related to or caused by fermentation) and septic fevers. As aforementioned, they may also experience symptoms of typhoid and influenza.12

As discussed above, the primary health condition for which the homeopathic remedy Pyrogenium is used most frequently is to treat blood poisoning and related symptoms. This homeopathic medicine has the potential to provide relief as well as cure symptoms like cold sweats, high fever, irregular pulse rate as well as restiveness. In addition, Pyrogenium has the aptitude to relieve common pain, while physical injuries as well as pains too can be alleviated by administering this homeopathic medicine. Pyrogenium solution is especially useful for treating ulcers, which are predominant among the aged people.12
In conventional medicine, people enduring these symptoms would generally be treated with penicillin or other comparable medicines that are able to fight infection. 12

In homeopathy, Pyrogenium is usually prescribed for patients who have an enduring history of sepsis and have not recovered from the condition completely. Mild lesions as well as inflammations too can be cured using Pyrogenium solution. In addition, this is considered to be among the most effective remedies for bacterial infections. 12

In addition to the above mentioned conditions and associated symptoms, the homeopathic remedy Pyrogenium is also effective in curing problems of the liver, the kidneys, bowels, urinary tract, gallbladder and lungs. It may be noted that this homeopathic medicine is also prescribed to treat skin disorders. Particular types of fevers can also be cured by administering Pyrogenium - for instance, ptomaine fever, typhoid fever and any other fever that develop bit by bit. In fact, this homeopathic medicine has also been found to be effective in treating sinusitis and nasal congestion. Besides, additional problems related to the nose, including headaches, burning sensations and/ or discharges may also be cured using this
homeopathic remedy. Significantly enough, Pyrogenium has also been given to pets suffering from high fever, discharges or weak pulse rate.  

Here is a word of caution. Taking large doses of Pyrogenium or existence of the substance in excessive amounts in the body may result in severe health problems. In fact, taking large doses of this medicine may cause blood damage similar to poisoning of the blood. It may be noted that the use of Pyrogenium ought to be stopped in case the patient experiences a deterioration of the symptoms or if his/ her condition does not show any sign of improvement even after days of using this homeopathic medication. In addition, pregnant women and nursing mothers should essentially seek medical advice before using this homeopathic remedy.  

While Pyrogenium is generally available in liquid form, the patients are mostly prescribed the pellet or tablet form of the medication. Generally, the pellet and tablet forms of this homeopathic remedy dissolve easily in the mouth. It is essential to take the medicine doses within 10 minutes of taking a meal. Moreover, this homeopathic medicine ought to be stored in a cool and dry place with the bottle containing it being adequately sealed. It may be underlined that any form of Pyrogenium medicine that is available without a seal or with a kaput or tampered seal should never be used.
2.4.12.1 Source: Beef/Septic Pus

2.4.12.2. Parts Used

The solution left behind after filtering, evaporating and watering down a mixture of lean beef and water is used to prepare the homeopathic remedy pyrogenium.

2.4.12.3. Uses

The homeopathic remedy Pyrogenium primarily influences the blood and, hence, it is generally used to treat blood poisoning symptoms. Such symptoms of blood poisoning may include high fever and sweating, wherein the pulse is unusually fast in comparison to feverish conditions. In addition, people suffering from blood poisoning may experience severe bone aches and may have a sensation as if the whole body is injured. They also experience extreme restiveness and their tongue becomes dehydrated, red, cracked and glistening.

In homeopathy, Pyrogenium is generally administered to treat septic conditions or cases wherein there is a history of sepsis (a serious localized or general infectious condition) from which the patient has never recovered completely. Occasionally, the patient may experience violent burning sensations, for instance, in accompaniment of an abscess. In such cases, all discharges from
the body are extremely offensive or contagious. All such symptoms may be
effectively treated by administering the homeopathic remedy Pyrogenium.  

The concept and even the attempt to use substances derived from one
organism to kill another organisms (antibiosis) are almost as old as the science of
bacteriology. (E.g. mouldy curd of Soya bean applied to boils). This is in one-way or
the other resembles homoeopathic law “Similia Similibus Currenter” i.e. likes
are cured by likes.  

The Scientists Pasteur and Joubert 1877 confirmed this, they noted that
anthrax bacilli grew rapidly when inoculated into sterile urine but failed to
multiply and soon died if one of the “common” bacteria of the air was introduced
in urine at the same time. With the breakthrough invention of the antibiotic,
Penicillin, which is derived from Penicillin Notatum, a mould, shown by
Alexander Fleming in 1928, death due to infectious disease drastically came down.
Since then newer antibiotics came into the market and proved to have excellent
therapeutic potential in curing the pathogenic manifestations. But amongst all this,
drug resistance has become a menace for medical science. Since adaptation is
quality of life and by mechanism of mutation, transformation, transduction &
conjugation many bacteria have become resistant to antimicrobial drugs.
Optimal and judicious selection of antimicrobial agents for the therapy of infectious diseases requires clinical judgment and detailed knowledge of pharmacological and microbiological factors. The diagnosis may be masked if appropriate cultures are not obtained prior to therapy. Antibiotics can cause serous toxicity and injudicious use of antimicrobial agents promotes selection of resistant microorganisms. For definitive therapy the regimen should be changed to a more specific (narrow spectrum) antimicrobial agent once an organism has been isolated and results of susceptibility tests are known.\textsuperscript{6}

It is proven beyond doubt that due to inappropriate and unethical use of antimicrobials, apart from drug resistance, generation of new mutant forms of non-pathogenic bacteria is posing a severe threat to the medical science (e.g. Non-pathogenic E.Coli has become pathogenic, once known for its symbiosis is now responsible for a wide range of Gastro-intestinal infection & Urinary tract infection pathologies.\textsuperscript{11}

Now host defense mechanism is the most important determinant of therapeutic effectiveness. Therefore stimulating ones immune mechanism would be more appropriate tool in combating the raising incidence of infectious diseases\textsuperscript{(11)} drug resistance and mutation.
Although to kill bacteria is not our aim since bacteria are not cause of disease, but disease lies in person himself (i.e. susceptibility) and bacteria is merely a secondary cause. In the wonderful science of Homoeopathy of defense mechanism is done by minuteness of Homoeopathic drugs, as Arndt-Shultz law States that “Large doses kill; Moderate dose inhibit; and small doses stimulates”. (6)