LITERATURE REVIEW
REVIEW OF LITERATURE

The use of many indigenous medicinal plant preparations and medicaments was well known to ancient physicians of India. Later on the Ayurvedic and Unani physicians also used different preparations of these plants in the treatment of various ailments. However, the effects of various preparations of indigenous medicinal plants had not been scientifically investigated and documented till the beginning of this century. The pioneering monumental work of Sir Ram Nath Chopra and colleagues aroused a great deal of interest of researchers in the field of indigenous medicinal plants of India.

Subsequently, large number of investigators started carrying out studies on different aspects of many medicinal plants. At least 2500 different plants which have been used in the traditional system of medicine have been shown to exhibit various types of pharmacological actions. However, it is apparent from the following brief review of research on medicinal plants that greater emphasis has been laid on search for plants with pharmacological actions on Central Nervous System (CNS), Cardio-Vascular System (CVS) and antifertility activity followed by those with anticancer, hypoglycemic, antinflammatory and antimicrobial activity. In the past there have been only few examples of researches on biochemical effects of these plants. Recently, the
effects of these medicinal plants on clinically important biochemical parameters of blood and urine have been studied in the normal rabbits and human subjects\textsuperscript{20-23}.

A concised up to date review on systematic research on medicinal plants revealing important aspects of their pharmacological and biochemical action is presented here\textsuperscript{24,25,26}.

**PLANTS WITH PREGNANCY INTERCEPTIVE ACTION:**

Recently, there has been exhaustive review on research on Indian Medicinal plants with interceptive activity\textsuperscript{27}, 120 plant species belonging to 103 genera and 54 families have been mentioned to be emmenagogue or/and abortifacients in the ancient Indian literature. 48 plants species covering 43 genera and 32 families have been tested for anti-implantation activity. In addition, 65 plants species belonging to 59 genera and 37 families not mentioned in the traditional literature were tested for anti-implantation activity. It was revealed that 21 plants mentioned in ancient texts and 19 plants not listed in the old literature showed activity as per shown in the subheadings of plants with antiimplantation and abortifacient activity. These observations suggest the necessity for random screening of all the available plants for fertility regulation. Also there have been variations in their reports (from inactivity to 100\% activity) of the same plant part by different
investigators\textsuperscript{28-33}. Moreover, the clinical data on antifertility plants are meagre. Therefore, the reviewers suggest adoption of systematic approach as advocated by WHO and ICMR task force for evaluation of fertility regulating plants to generate reproducible results.

**PLANTS WITH ANTIMPLANTATION ACTIVITY:**

Among the listed plants in old literature whose recommended parts have been tested and showed more than 50\% antiimplantation activity are *Abroma agusta\textsuperscript{34}, Butea frondesa\textsuperscript{35}, Carica papaya\textsuperscript{36}, and Daucus carota\textsuperscript{37}*. Plants showing more than 50\% anti-implantation activity in experimental animals but have not been mentioned in the old literature are *Datura quercifolia\textsuperscript{38,39}, Pueraria tuberosa\textsuperscript{40} and Rubus ellipticus\textsuperscript{41}.*

The pure compounds isolated from different medicinal plants showing anti-implantation and other activities are as follows:

<table>
<thead>
<tr>
<th>Name of compound</th>
<th>Source</th>
<th>Estrogenic properties</th>
<th>% Antiimplantation activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cerenaridine</td>
<td><em>Tabernaemon tanaheyneana</em>\textsuperscript{42}</td>
<td>Estrogenic</td>
<td>100</td>
</tr>
<tr>
<td>2. Daturalactone</td>
<td><em>Datura quercifolia</em></td>
<td>Estrogenic</td>
<td>73</td>
</tr>
</tbody>
</table>


PLANTS SHOWING ABORTIFACIENT ACTIVITY:

Such plants have been found to be intestinal irritants and produce violent gastro-enteritis causing contractions and abortion. About 23 plants of 23 genera and 21 families have been screened for their abortifacient activity. Of these 13 plants have been mentioned in the ancient literature for abortifacient property. *Azadirachta indica* and *Carica papaya* exhibited 100% pregnancy interceptive activity. The remaining plants *Adhatoda vasica* and *Ensete superbum* showed significant interception of pregnancy. At present, one abortifacient plant *Adhatoda vasica* is under clinical trial. *Carica papaya* demands attention for its followup and clinical trials.

RESEARCH ON PLANTS WITH CENTRAL NERVOUS SYSTEM (CNS) ACTIVITY:

The plants described to have CNS activity have gained considerable interest of the researchers in the recent
years. Among the large number of medicinal plants exhibiting CNS depressant action, the important ones are as follows:

Cichorium intybus roots showed anticonvulsive property\(^{48}\). Isococculidine, a quaternary alkaloid-isolated from the leaves of *Cocculus laurifolius*\(^{49}\) has been demonstrated to exhibit mild neuromuscular blocking activity. Similar to the action of caffeine, the essential oil of *Psoralea corylifolia* is reported to be stimulant of skeletal muscles\(^{50}\).

*Zizyphus jujuba* and *Euphorbia neriifolia* have been reported to exert local anaesthetic activity\(^{51}\) where as *Morus indica* showed potent local anaesthetic and analgesic activity\(^{52}\). Interpenic acit, isolated *Corchorus depressus* has been shown to have both analgesic and antipyretic activity\(^{53}\) and *Desmodium polycarpum* have shown only analgesic activity\(^{54}\).

*Convolvulus pluricaulis* has been reported to exert significant tranquillising effect in animals and in clinical studies\(^{55}\). In rats, mild tranquillising effect has been shown to be exerted by essential oil of the rhizomes of *Hedychium coronarium* & *H. spicatum*\(^{56}\).

Significant adrenergic neuron blocking action is reported to be exhibited by epistephanine, isolated from *Stephania bernandilfolia*\(^{57}\). Similar to the pharmacological profile of
chlorpromazine, the dopamine receptor antagonistic action has been shown by nuciferine, isolated from *Nelumbe nucifera*, however, its Hofman degradation product, athero-sperminine, exerted the effects similar to dopamine receptor stimulation.

**Medhya Rasayana** drugs described in *Ayurveda* viz *Bacopa monnieri*, *Glycyrrhiza glabra*, *Convulvulus pluricaulis* and *Tinospora cordifolia* have been found to decrease the acetylcholine content of whole brain and cortex in stressed rats. Also there occurred decline in the whole brain histamine content however, cortical portion showed increase in histamine content.

The extract of *Withania somenifera* has been reported to potentiate barbiturate hypnosis, decline acetylcholine and catecholamines and raise the serotonin and histamine levels in whole brain.

In the past, much attention has been given to study the interaction of *Cannabis* with CNS depressants which have been confirmed in rats that most of the CNS activity of cannabis is serotonin-mediated.

**Echitovenidine** (major alkaloid of *Alstonia venenata* fruit) and strictamine (an indolic alkaloid isolated from *Alstonia scholaris* flower) have been reported exhibit MAO inhibitory activity. *Celastrus paniculatus* seed oil treated rats showed
an enhanced learning and memory process\textsuperscript{65}. \textit{Ocimum sanctum} which is reported to have antistress activity in the experimental animals modulates the humoral immune responses by acting at various level in the immune mechanism such as antibody production, release of mediators of hypersensitivity reactions and tissue responses to these mediators in the target organs\textsuperscript{66}.

**PLANT WITH ACTION ON CARDIOVASCULAR SYSTEM (CVS) HYPOLIPIDEMIC AGENTS:**

In last two decades the researches on \textit{Commiphora mukul} (Gum gugul) reveal it as a consistent potent hypolipidemic agent. It has aroused considerable interest in other medicinal plants for search of similar effect. Recently an Indian Pharmaceutical firm has marketed the drug \textit{Guggulipid}-a mixture of several steroid lipids as a potent hypolipidemic agent isolated from \textit{C.mukul} following its release by the Prime Minister of India in Jan. 1987\textsuperscript{67}. Onion has been reported to exert hypolipidemic effect in patients of ischaemic heart disease\textsuperscript{68} and in normal subjects of Jain community\textsuperscript{69}. Garlic pretreatment has been shown to reduce serum cholesterol in rabbits\textsuperscript{70-71} and rats and to protect rats against isoprenaline induced myocardial necrosis\textsuperscript{72}. Garlic extract feeding in rats prolonged the clotting time, bleeding time and recalcification time but led to a rise in peptic activity and mucin content of the gastric juice\textsuperscript{73}. Clinically,
raw garlic has been reported to lower the blood cholesterol in normal subjects\textsuperscript{74-75}. Recently odorfree garlic preparation has been shown to decrease total serum cholesterol, triglycerides, VLDL and increase the HDL-C and phospholipids in cases of non-insulin dependent diabetics\textsuperscript{76}. In the recent years many plants have been screened for its hypolipidemic activity\textsuperscript{23} to \textsuperscript{33}. \textbf{M. Charantia} has been reported to decrease total serum cholesterol, triglyceride, LDL and increase HDL-C and phospholipids in the normal albino rabbits\textsuperscript{23-24} and in the mild diabetics subjects it is reported to possese HDL-C and hypocholesterolemic and hypolipidemic action\textsuperscript{77}. \textbf{Ajawan, trigenella foenum graceum} (Methi) seeds and leaves and \textbf{Trichesonthes dioca} (Rexb) fruit and seeds have been found to lower the total serum cholesterol and increase the phospholipids and decrease the triglycerides\textsuperscript{25-33}.

\textbf{HYPOTENSIVE AND CARDIOTONIC AGENT}:

A large number of plants have been screened for their action on Cardiovascular system (CVS). Of these, more than 60 plants have been found to possess mild to moderate degree of hypotensive and cardiotonic activity. \textbf{Coleonol}, a di-terpene isolated from \textit{Coleus forskohlii}, is found to be potent hypotensive agent\textsuperscript{78}. \textbf{Crotosparine}, the N-methyl derivative of a proaporphin base from \textit{Croton sparsiflorus} has been reported to have good hypotensive activity\textsuperscript{13}, \textbf{Carica}
papaya has been shown to lower the blood pressure and paralyse the earthworm\textsuperscript{79}. Recently, scoparone (6,7-dimethyl esculetin) isolated from aerial part of Artemisia scoparia has been shown to cause prompt lowering of blood pressure in anaesthetized and conscious normotensive and hypertensive animals. It exerts its action by a direct vasomoter inhibition at the central site and also to cause marked peripheral vasodilation of the arterial blood vessels\textsuperscript{80}.

Buddleja asiatica showed persistent hypotensive activity in cats and dogs which was found to be due to an alfa receptor antagonistic action\textsuperscript{81}. Significant hypotensive action has also been revealed by other plants viz. Erythrina variegata\textsuperscript{82}, Hibiscus rosasinensis\textsuperscript{83}, Sapindus trifoliatus\textsuperscript{84}, Piper aurantiacm\textsuperscript{85} and Eclipta alba\textsuperscript{86}. E.alba has been reported to have myocardial depressent action. Asclepin, a new Cardenolide from Asclepin curassarica revealed cardiotonic activity in cats and guinea pigs which is comparable to digoxin and ouabain with a better margin of safety\textsuperscript{87}. Other important plants showing cardiotonic effects are Tribulus terrestris\textsuperscript{88} and Mollugocerviana which cause a sustained inotropic effect perhaps mediated through autonomic receptors\textsuperscript{89}.

ANTIMALARIAL ACTIVITY OF MEDICINAL PLANTS:

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\textbf{ANTIMALARIAL ACTIVITY OF MEDICINAL PLANTS}:

Many plants have been mentioned in the ancient
literature in Ayurveda and in the current literature (Medicinal plants of India Voln. I and II) which have been reported to possess antimalarial activity.

Of these, recently ethanolic extract of aerial parts of Xanthium strumarium, Atlantia monophylla, Eucalyptus globulus, Artemesia parviflora, Nycthanthes asbortristis, Exhinops echinatus, Ocimum sanctum, were tested for their antimalarial activity. The most effective extracts were Xanthium strumarium and Atlantia monophylla. They were effective on chloroquine resistant and chloroquine sensitive strains of Plasmodium falciparum. Some activity was observed with Eucalyptus globulus, Artemesia Parviflora, Nycthanthes asbortristis but E. echinatus and O. sanctum did not show any antimalarial activity.

PLANTS SHOWING HYPOGLYCEMIC ACTIVITY:

In the last decade, many plants have been shown to exhibit hypoglycemic activity. The hypoglycemic action of M. charantia is well known. Other important plants are Coccinia indica and Coccinia var. palmata, Zingiber efficianale, Cinamomum tamala, Inula racemosa, Terminalia belerica, Cymopsis tetragonoloba, Pterocarpus marsupium, Dipteracanthus prostratus, Pterocarpus santalinus, Rhus Chinensis and Trichosan
the \textit{palmata}, \textit{onion}\textsuperscript{97}, \textit{Trichosanthes dioca}\textsuperscript{30} and \textit{Carum copticum}\textsuperscript{26}.

\textbf{Many leguminous} plants of the Acacia family have also been reported to exert hypoglycemic action in experimental diabetes\textsuperscript{98}. Of these, the important ones are \textit{Glycine soja}\textsuperscript{99}, \textit{Delichos biflorus}, \textit{Circera Arietinum} and \textit{Mucuna pruriens}\textsuperscript{100}. \textit{Azadirachta indica} showed \textit{hypoglycemia} as well as \textit{antihyperglycemic} effects in dogs with adrenaline induced and glucose induced \textit{hyperglycemia}\textsuperscript{101}.

\textbf{Fenugreek} (Trigonella foenum graceim) seeds have been found to lower blood glucose levels where serum insulin levels were also modified to a similar extent in human subjects\textsuperscript{102}.

Epicatechin-A flavonoid isolated from \textit{Pterocarpus marsupium} has been found to exert antidiabetic action by promoting regeneration of the beta cells of the pancreas\textsuperscript{103}. However, the later reports by the investigators have not been confirmed for such activity of epicatechin\textsuperscript{104}.

\textbf{PLANTS WITH HYPERGLYCEMIC EFFECT}:

In the literature, \textit{Canabis} has been shown to cause a significant \textit{hyperglycemia} with simultaneous fall in liver glycogen in rats\textsuperscript{61-63}.
PLANTS EXHIBITING ANTIBACTERIAL ACTIVITY:

Essential oils and different preparations of several plants have been reported to show antibacterial activity against gram positive and gram negative bacteria. Among such plants are Oenanthe javanica\textsuperscript{105}, Carica papaya\textsuperscript{106}, Laggera aurita, Blumea membranacea, Caesulia axillaus, Cythochline lyrata, palma rosa and Psoralea corylifolia\textsuperscript{107}. Two alkaloids isolated from Evodia lunuankenda exhibited antibacterial activity\textsuperscript{13}. Carpain isolated from Carica papaya has been found to be active against certain gram positive and gram negative bacteria as well as active against some species of yeast. Also it is highly active against Bacillus cereus and moderately active against B. mycoid\textsuperscript{108}. Recently, antibacterial substance from C. papaya fruit extract has been reported\textsuperscript{109}. Crude extract of Allium sativum (Garlic) have been reported to significantly inhibit the growth as well as production of Enterotoxins in E.coli\textsuperscript{110}.

PLANTS WITH ANTHELMENTIC ACTIVITY:

Many plants have been found to exhibit mild to moderate anthelmentic acitivity. Of these, the importat plants are Carica papaya, sapindus trifoliatus, Butea frondosa and Momordica charantia\textsuperscript{111}. In vitro screening of several plants of different families against human round worms have revealed that the plants of the Zingerberacease family
possessed potent activity\textsuperscript{112}. \textbf{Melia azadirachta} (neem) are clinically effective against ascariasis\textsuperscript{113} and \textbf{Caesalpinia crista} seeds against human amoebiasis\textsuperscript{114}.

**PLANTS WITH ANTIFUNGAL ACTIVITY**

<table>
<thead>
<tr>
<th>PLANTS PREPARATIONS/COMPOUNDS/ PARTS</th>
<th>FUNGISTATIC FUNGICIDAL CES</th>
<th>ANTIFUNGAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Mucuna Puriens</td>
<td>Ether &amp; Chloroform extract of seeds</td>
<td>115</td>
</tr>
<tr>
<td>2. Curcuma longa</td>
<td>Stem</td>
<td>&quot;</td>
</tr>
<tr>
<td>3. Shorea robusta</td>
<td>Ether extract of Resin</td>
<td>Fungicidal</td>
</tr>
<tr>
<td>4. Azadirachta-indica</td>
<td>Chloroform extract</td>
<td>&quot;</td>
</tr>
<tr>
<td>5. Pongamia glabra</td>
<td>Chloroform extract</td>
<td>&quot;</td>
</tr>
<tr>
<td>6. Curcuma amada</td>
<td>Rhizomes</td>
<td>Invitro</td>
</tr>
<tr>
<td>7. Cascia alata</td>
<td>Plant</td>
<td>Potent antifungal</td>
</tr>
<tr>
<td>8. Saussurea lappa</td>
<td>Plant</td>
<td>&quot;</td>
</tr>
</tbody>
</table>

Many chemical constituents have been isolated from the medicinal plants which showed potent antifungal activity viz. a flavonoid from \textbf{Alpimia officinarum}, \textbf{Schiwallina}-asaponin from \textbf{Schima vallichii}\textsuperscript{119}. \textbf{Embodin} from \textbf{Rumex maritimus}\textsuperscript{120}, a number of antidermatophytic constituents
i.e. lactones, alantolactone and isoalanto-lactone from *Inula racemosa*\textsuperscript{121} and arnebin from *Arnebia nobilis*\textsuperscript{122}.

**ANTIVIRAL ACTIVITY:**

Antiviral activity of several plants has been confirmed. Among them, important medicinal plants belong to 14 major genera viz. *Acacia*, *Argyreia Cassia*, *Ficus*, *Greina Ipomea*, *Litsea*, *Euphobia*, *Piper*, *Polygenum*, *Solanum simploces*, *Quercus* and *Z.1syphus*. Barberin chloride eye drop is reported to have curative effect in clinically positive cases of trachema. The antiviral activity is said to be due to the presence of interferon like substances in these plants\textsuperscript{124}.

**ANTI-CANCER ACTIVITY:**

Active constituents of at least 15 plants have been isolated, characterised and biologically evaluated for their anti-cancer activity. Of these, most potent biogically active antitumour agent from *Cocculus pendulus*, *Roylea Calvcina* and *Tephrosia candida* have been characterised\textsuperscript{13}. Other plants with varying degree of antitumour activity are *Allium cepa*\textsuperscript{125}, *Rhazya stricta*\textsuperscript{126}, and *piospyros montana*\textsuperscript{127}.

The anti-viral and anti-toumer activities of *Cassia fistula*, *Algaia rexburghiana* and *Zingiber capitatum* is attributed to the presence of interferon like substances in
them$^{128}$, and sesquiterpene lactone components from *Parthenium hysterophorus* and *plumbagin* from *plumbago rosea* in *chick embryos*.$^{129}$

**ANTI INFLAMMATORY ANALGESIC AND ANTIPYRETIC ACTIVITY OF MEDICINAL PLANTS:**

Several medicinal plants have been reported to show anti-inflammatory and analgesic activity and active derivatives of some plants have also been isolated and biologically tested. Of these, most important ones are *Calophyllum inophullum* and *Mesua ferrea* and their xanthothes$^{130}$ and also a *coumaria* derivative *calophyllide*.$^{131}$ In a clinical trial on patients of definite rheumatoid arthritis curcumin (diferuloyl methane) showed a more significant improvement.$^{132}$ In comparison to *phenylbutanzone*. **Potent analgesic**, anti-pyretic and anti-inflammatory activities in rats and mice have been shown by *Hibiscus rosa sinensis*, *Nerium indicum* (Glycoside), *Withania somnifera*.$^{133}$ About 29 plants have been shown to possess anti-inflammatory activity.$^{13}$

**ANTI ULCER ACTIVITY OF PLANTS:**

Curcumin is well known for its effect on the gastric mucosa and secretions and reported to possess antiulcer activity.$^{134}$ Triterpenoids (ulsolic acid and lupeol) from a number of Indian medicinal plants belonging to sapotaceae/
-sapindacease family evinced antiulcer activity in rats subjected to restraint stress. Alcoholic extract of *Tectona grandis* significantly inhibited restraint ulcers in rats and histamine-induced ulcers in guinea pigs. *Emblica officinalis* (Amlaki) has been found to provide relief in dyspepsia. *Wimalawansa* has reported the efficacy of papaya in the treatment of chronic infected ulcers. *Chan et al.* have shown the protective effect of *carica papaya* on the exogenous gastric ulcers in rats.

**SPASMOLYTIC AND ANTI SPASMODICA EFFECTS:**

Number of plants have been reported to exhibit these activities of varying degree. Among these *Clausena pentaphylla* and *cedrus deodara* have been found to be highly potent. The active constituents have been reported to be clausmarin a new coumarin, and sesquiterpenoid respectively diseases showed significant improvement in cough and expectoration without any significant reduction in air way resistance.

**PLANTS WITH DIURETIC ACTIVITY:**

Several plants have been mentioned in our old literature for their diuretic action. Currently, many plants have been tested for their diuretic activity. Among these most important plants are extracts of *Cardiospermum helicacabum* and
Minosa pudica. A dose dependent saluretic effect without affecting the potassium excretion is shown by Cucumis trigonus. Three new coumarins and an alkaloid have been isolated from Toddalia asiatica showing diuretic action. Cractava nurvala has been shown to be an Ayurvedic drug of choice in the treatment of various urinary disorders and helps in the migration of stone and preventing atony of bladder, following prostatectomy, carpain-an alkaloid isolated from C. papaya has also been listed as diuretic.

PLANTS ACTING ON HEPATIC FUNCTIONS:

More than 90 plants have been mentioned in our old literature to be beneficial in the treatment of liver diseases. Among them the most important one investigated are Luffa chinata, Nymphoea stellata, Withania Somnifera, Indigofera tinctoria, Ricinus communis have shown protection against CCl₄ induced hepatic damage in rats.

Nymphoea stellate, Withania somnifera, Indigofera tinctoria and Andrographis paniculata increased the bile flow and liver weight probably by stimulating liver microsomal enzymes. Kutikin-the isolated iridoid glycoside mixture of Picrorhiza kurrooa has been found to possess significant hepatoprotective effect in rats.
**Luffa echinata** fruit juice administered as nasal drops to patients of viral hepatitis led to a reduction in serum bilirubin and serum glutamic pyruvic transaminas along with substantial relief in clinical symptoms like **anorexia** and **malaise**. There was profuse **rhinorrhea** following instillation of **L. echinata** drops in the nose, the nasal secretions contained 1.6 to 5.5 mg% **bilirubin**\(^\text{150}\).

In a pilot study, two well known medicinal plants **Eclipta alba**, and **Phyllanthus niruri** inactivated hepatitis-**B-antigens** (HBs Ag) in **vitro**\(^\text{151}\).

However, the plants mentioned to act on hepatic functions remain largely unexplored and the research on these plants, which might improve hepatic function, would be useful addition to modern therapeutics.

**PLANTS SHOWING ADOPTOGENIC AND ANABOLIC EFFECTS:**

Only certain drugs mentioned in the Ayurveda have been tested for their effect on the process of ageing. In a clinical study, as compared to placebo, the administration of **Withania somnifera** root powder in milk for one year in human subjects aged 50-59 years has shown significant improvement in several biochemical parameters of blood\(^\text{152}\).
Also administration of W. somnifera alone and in combination with *Boerrharia diffusa* with milk to normal children aged 8-12 years showed a significant increase in body weight, total proteins and mean corpuscular haemoglobin concentration\textsuperscript{153}. *Boerrharia diffusa* (Punernava) whole plant powder also promoted a positive nitrogen balance, growth and longevity in albino rats on stock diet which was not so marked in animals on a low protein diet\textsuperscript{154}.

*Embeliaca officinalis* administration for one year to 36 ophthalmic patients has been reported to be effective in delaying the pathological changes characteristic of senile maculopathies \textsuperscript{155}.

*Bauhinia variegata* (Kachnar) and *Jalkumbhi* were found to possess beneficial effects in experimental goitre in rats\textsuperscript{156}.