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Significance of Plant Bitters In The Field of Pharmacognosy

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ABSTRACT

Bitters are imperative; everyone needs some bitters in their diet. No traditional culture could have imagined a diet virtually devoid of any bitter foods—as we seem to have established in most modern diets. The quality of a plant's bitterness is widely variable in both character and degree. Many bitter herbs are more accurately referred to as foods, while others are decidedly medicinal in their action. Bitter foods should be considered essential to good nutrition, whereas bitters of a more medicinal nature should be reserved to address specific concerns not remedied by dietary bitters. The bitters have been proven to be effective in curing all allergic, metabolic and immunological conditions where the diagnosis points to the digestion.

Key-words:
plant bitters, appetite, bitters food etc.

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INTRODUCTION

What seems to us as bitter trials are often blessings in disguise.

~Oscar Wilde

Plants are integral part of human civilization. Medicinal plants are also been relied upon by over 80% of the world population for their basic health care needs.

The universality and efficacy of traditional medicine/ medicinal herbs is evident in their continued use and dependence up till the present day by a significant portion of the world's population.

In modern herbal medicine, bitter principles occupy a central place in herbal therapeutics beating the acrid constituents. Most people consuming herbal medicines complain about the bitterness of the medicines prescribed. This is the only defining attribute of herbal medicine and the only feature to set it apart from other therapies.

Bitter refers to the plant nature of being and tasting bitter. Bitters are the edible natural products mostly consumed before any normal meals to stimulate as well as enhance the appetite. However, the bitter glycoside as a class does possess almost similar activities like the bitters such as: digestive, stomachic and febrifuge. The quality of a plant's bitterness is widely variable in both character and degree. Many bitter herbs are more accurately referred to as foods, while others are decidedly medicinal in their action. Bitter foods should be considered essential to good nutrition, whereas bitters of a more medicinal nature should be reserved to address specific concerns not remedied by dietary bitters.

Bitter is popular name for alcoholic drinks which combines the properties of appetizer and tonic.

Generally combined with gin or vermouth they are ingredient of cocktail. Bitters are tincture or extract of bitter aromatic herbs like angotura or bitter orange.

Bitters are a heterogeneous group of naturally occurring compounds, marked by their strong bitter taste and therapeutic importance rather than a chemical classification.

Or

In general, the bitter principles are heterogeneous vegetative compounds that neither belongs to the class of *alkaloids* nor to the *glycosides,* but they do possess a characteristic bitter taste.[1]

Bitters are imperative; everyone needs some bitters in their diet. No traditional culture could have imagined a diet virtually devoid of any bitter foods—as we seem to have established in most modern diets. Traditional herbalism in cultures throughout the world considers bitters to have a "downward" action. This refers not only to bitters more readily perceived digestive actions (including their admirable efficacy in resolving bad breath arising from the gut), but also to their more esoteric virtues[1].

CLASSIFICATION

The classifications of bitter plants on the basis of their chemistry are as follows-

CHEMICAL CLASSIFICATION OF BITTER PLANTS[2]

Sr no	Chemical class	Bitter compound	Plants
1	Glycoside	Gentiopicroside (Gentiopicrin, Gentiamarin), Amarogentin, PicrosideI &II, Kutkoside, Sweroside and swertiamarin, Amaroswerin, picrocrocin	Gentian, picrorrhiza, chirata
2	Alkaloid	Quinine, Quinidine, Cinchonine, Cupreine, Hydroquinine, Strychnine, Brucine, Aristolochic acid ,Boldine or Boldoin Hydrastine, Berberine and Canadine Calumbin, Palmatine, Jatrorrhizine Ophioxylin, Reserpine	Cinchona,Nuxvomica, Serpentary, Boldo, Hydrastis, Calumba, Barberry, Rauwolfia Gold Thread

3	Diterpene	Andrographolides,taxanes	Kalmegh,texus
4	Triterpene	Quassin, neoquassin	Quassia
5	Sesquiterpene	Santonin, absinthin,artabsinolide,taraxacin	Dandelion, chamomile, Worm wood
6	Flavonoids	Silybin, silydianin, silychristin, quercitrin, quercetin, kaempferol	Silymarine, hypericum
7	Tanins	Quercitannic acid, quercin	Oak, bayberry

ROLE OF BITTERS [3]

Bitters stimulate all digestive secretions: saliva, acids, enzymes, hormones, bile, and so forth. Each of these acts as a solvent to break down food for absorption, and the quantity and quality of these fluids ensure proper nutrition. Inadequate production of these secretions is common in modern cultures (i.e. cultures lacking bitters in their diet), and the implications of such deficiencies are myriad. When first tasted, bitters promote salivation, which begins the process of digestion by breaking down starches and beginning to work on fats. Taste receptors in the mouth (there are over twenty-five different bitter taste receptors) recognize the presence of bitters, and trigger a system-wide reaction throughout the digestive tract.

Bitters act as appetizers

Gastrin is known to be very effective in increasing the appetite. It acts directly on appetite centres in the hypothalamus and indirectly through increased stomach motility. As we have seen earlier, bitters have also been used as key elements in aperitifs or for increasing appetite during convalescence. They can be very useful indeed in treating anyone for whom anorexia is posing an obstacle to recovery. Sometimes, lack of appetite is the body's own signal to prevent overstuffing. But this type of anorexia should be distinguished from other harmful types that reduce the strength of an individual. Administering bitters then comes in quite handy and especially in case of anorexia nervosa where bitters are a very helpful tool to counter the problem.

Bitters increase secretion of digestive juices

Bitters are known to expedite the process of digestion by boosting the stomach and pancreatic enzyme secretions. In those cases where these secretions are irregular or malfunctioning, bitters can help a lot towards speedier digestion by breaking down the food material. Digestive secretions sterilize the food material inside the stomach and break down protein and other large molecules that threaten the body's immune system. There is a paradox with food. It is certainly the most important source of nourishment for the body, but it also poses the greatest immunological threat to it. This is reflected in the presence of lymphoid tissues in the digestive tract. The digestive juices denature the antigenic material that prevents the situation from going out of control. Herbal therapeutics point out that a fall in digestive secretion can damage the body to a great extent. It should always be corrected immediately as and when encountered. Besides enteric infections and food allergies, such reduced ability to digest can be understood by the symptoms of a nauseous feeling, or feeling bloated even after taking a little food. Passing small malodorous stools is another sign. As modern food items contain an increased percentage of adulteration, the risk of depressed digestion has increased greatly, and the only measure is to administer bitter remedies.

Bitters offer protection to the gut tissues

In cases of heartburn, hiatus hernia or oesophageal inflammation, the reflux of corrosive stomach contents into the oesophagus is prevented by bitter remedies. This task is achieved by increasing the tone of the gastro-oesophageal sphincter. The bitters also decrease the harmful effects of the digestive juices and dietary toxins by enhancing the already rapid rate of mucosal regeneration in the stomach and duodenum. This acts as a healer in the case of ulceration or an infection. Similar action, if performed on the matrix of the pancreas might as well help in pulling through a pancreatic disease.

Bitters enhance bile flow

Bile juice is secreted by the liver. It is also considered as the excretion of liver. The liver contains extremely dynamic flow of juices. If pictured, each cell can be seen as being in a stream of a mixed nutrient-rich portal blood from the gut and oxygen-rich arterial blood from the general circulation. These fluids disseminate through the cell, and are subjected to heavy dispensation that is a part of the liver function. The metabolic products that are born out of this activity move from the liver cell into the outgoing blood flow. Some of the most important, however, are channelled into a separate exit that drains into the biliary system. The liver thus self-cleanses by its own mechanism.

The bitters have been proven to be effective in curing all allergic, metabolic and immunological conditions where the diagnosis points to the digestion. The liver exerts an influence over the immunological system as well. Even in case of herbal therapies for migraines hepatic remedies are suggested, most of which use the bitter. The use of bitters leads to a greater production of biliary elements and dilutes the bile as well by increasing the bicarbonate content. In case of gallstone formation or gall-bladder disease, that is formed by the over deposition of bile, bitters are known to work wonders. Along with lemon juice which dilutes the bile as well, bitters are also an effective and accepted treatment of these diseases.

Bitters improve pancreatic functions

Gastrin helps pancreatic secretion and also increases the secretions of insulin and glucagon, the two main hormones the pancreas produces. However, these are conflicting in nature. There is a possibility of a 'state dependent' effect. This is a response to gastrin that varies according to the condition of mutual and simultaneous secretion of the two hormones. Bitters have also been used in controlling late-onset diabetes. Chinese physiology states that bitters can effectively reactive hypoglycaemia and produce immediate and excellent results. Thus we conclude that bitters neutralize pancreatic hormone secretions by increasing the amount of glucagon when insulin is high and vice versa. They are more likely to raise a hormone level when it is deficient. Bitters control fluctuations in blood sugar levels permanently and temporarily as well.

Bitters act as tonics

All the above contributions of bitters make it easy to understand that they can boost your health to a great extent. Their primary role is to stimulate all the above mentioned digestive functions. The digestive processes are the platform where the nourishment requirements of the body are met. This is the place where the body examines the materials it is fed with and most calorific and metabolic processes are regulated. Depending upon the extent to which this platform is in danger under the modern living conditions, it might or might not respond to the bitter remedies. Bitter remedies were mainly resorted to in old age or in a convalescent state in order to be able to improve the quality of nourishment to the body. However, in the modern age, as illnesses become chronic in nature and more frequent, attacking persons of all ages, it is advisable to resort to bitter remedies. Food has also become less wholesome and more prone to indigestions. Bitter remedies can definitely offset the harmful effects of adulteration to a great extent.

Bitter Foods and Bitter Medicines

The quality of a plant's bitterness is widely variable in both character and degree. Many bitter herbs are more accurately referred to as foods, while others are decidedly medicinal in their action. Bitter foods should be considered essential to good nutrition, whereas bitters of a more medicinal nature should be reserved to address specific concerns not remedied by dietary bitters.

The very notion of having salad before a meal originates from the role of the bitter greens that were once the mainstay of salads. Indeed, salad wasn't always chopped iceberg lettuce and fatty dressings, but used to be made from wild leafy herbs such as dandelion and chicory, or many of the common weeds that naturally spring up around human habitations. These nutrient-rich herbs were complemented by vinegar dressings, which also serve to extract their minerals for optimal absorption. A salad of this nature not

only serves as a nutritious appetizer, but also aids in the digestion of heavier foods, which often make up the "main course" of meals. Medicinal bitters are too powerful in flavor to make useful foods. Few indeed (even me) would care to sit down to a soufflé of gentian roots, or replace their tarragon (*Artemisia dracunculus*) with wormwood (*Artemisia absinthium*). Such herbs are appropriately used to address a particular need, be it chronic indigestion or that heavy, stuffed feeling that often follows liberal holiday feasting.

Various bitter drugs and their constituent with uses

S.N.	PLANTS	BOTANICAL NAME	PART USED	CONSTITUENTS	USES
1	CINCHONA[1]	*Cinchona calisaya, C.ledgeriana, C. officinalis,* Family- Rubiaceae	Dried bark.	Quinine, Quinidine, Cinchonine, Cupreine, Hydroquinine	Antimalarial and antiarrythmic drug
2	NUXVOMICA [2]	*Strychnos nuxvomica* Family- Loganiaceae	Dried ripe seeds	Strychnine, Brucine,	Erectile dysfunction and anemia
3	SERPENTARY[3]	*Aristolochia reticulate* Family-Aristolochiaceae	Dried rhizome and roots	Aristolochic acid,	Local and general stimulant and tonic property
5	BOLDO[6]	*Peumus boldus*(Molino) Family- Monimiaceae	Leaves bark	Boldine or Boldoin,Volatile oil	Liver disease and uti andin dyspepsia
6	HYDRASTIS[1]	*Hydrastis Canadensis* Family-Berberidaceae	Dried rhizome and roots	Hydrastine, Berberine and Canadine	Atonic dyspepsia ,gastritis and jaundice
7	CALUMBA[3]	*Jateorhiza palmate* (J. calumba) Family-Minispermaceae	Dried sliced root	Calumbin,Palmatine,Jatrorrhizine	Diarrhoea and intestinal gas
8	RAUWOLFIA[3]	*Rauwolfia serpentiana* Family-Apocynaceae	Dried rhizome and roots	Ophioxylin,Reserpine	Sedation, hypertension, bradycardia
9	BARBERRY[3]	*Berberis vulgaris* Family-Berberidaceae	Bark,Berries	Berberine	Giardiasis and vaginal yeast infection
10	GENTIAN [3]	*Gentiana lutea* Family-Gentianaceae	Rhizome and root	Gentiopicrin,Gentisic acid,Gentianose,Amrogentin,Amaroswerin,Gentioside	Apetite, heartburn, vomitingand as germ killer
11	PICRORRHIZA[3]	*Picrorrhiza kurroa* Family-Scrophulariaceae	Dried rhizome	Picroside-I,II and Kutkoside	Cardiac and cerebral tonic, anthelmintic
12	CHIRATA[3]	*Swertia chirata* Family-Gentianaceae	Entire herb	Chiratin, Amarogentin, Ophelic acid	In BP as tinctures and infusions
13	QUASSIA[1]	*Picrasma excelsa* Family-Simarubaceae	Dried stem wood	Quassin,Neoquassin,Picrasmin	Anorexia, constipation and fever
14	KALMEGH[3]	*Andrographis paniculata* Family-Acanthaceae	Dried leaves and tender shoots	Andrographolide,Kalmeghin	Antihelmintic and cholera

15	ANGOSUTRA[3]	*Cuspari febrifuga, Galipea officinalis* Family-Rutaceae	Dried Bark	Angosturin,Galipene,Cusparine,Galipidine,Cusparadine	For flavouring beverage and food
16	CENTAURY[3]	*Erythraea cantaurium* Family-Gentianaceae	Herb and leaves	Erythrocentaurin	Blood purifier and excellent tonic
17	DANDELION[3]	*Taraxacum officinale* Family-Compositae	Fresh and dried root,Herb	Taraxacin	Loss of apetite , joint pain and eczema
18	OAK[3]	*Quercus robur* Family-Cupuliferae		Quercitannic acid,Quercin	Cold fever, cough and bronchitis
19	TULIP TREE[3]	*Liriodendron tulipifera* Family-Magnoliaceae	Bark	Iriodendrin,Tulipiferine	Anthelmintic, diuretic and nervine tonic
20	BALMONY[1]	*Chelone glabra* Family -Scrophulariaceae	Fresh Herb		Anthelmintic, antibilious and stimulant tonic
21	BAY BERRY[1]	*Myrica cerifera* Family-Myricaceae	Root, bark, seeds	Tanin,Saccharine	Intestine colitis, nausea and diarrohea
22	BOGBEAN[1]	*Menyanthes trifoliata* Family-Gentianaceae	Herb	-	To cure dyspepsia and torpid liver
23	CH AMOMILE[1]	*Anthemis nobilis, Chamomilla officinalis* Family-Compositae	Herb	Anthemic acid,Tannic acid	Insomnia, headache, digestive complaints
24	FRINGE TREE[1]	*Chionanthus virginicus* Family- Oleaceae	Root bark	Chionanthin.	For liver and gall bladder disorder
25	GOLD THREAD[3]	*Coptis trifolia* Family-Ranunculaceae	Dried rhizome with root stem and leaves	Berberine, Coptin	Digestive disorder and parasite infection
26	TANSY[2]	*Tanacetum vulgare,* Family- Compositae	Aerial parts	Apigenin,Luteolin,Chrysoeriol, Diometin	
27	SILYMARINE [2]	*Silybum marianum Family-Asteraceae (Compositae)*	Ripe seed	Silybin, silydianin, silychristin	
28	LIVER WORT[2]	*Lichen cinereus* terrestris,Family- Lichenes	Lichen		
29	FRINGE TREE[2]	*Chionanthus virginicus* Family- Oleaceae	Root bark	Chionanthin	
30	BOGBEAN[2]	*Menyanthes trifoliata* Family-Gentianaceae	HERB		

Chemical nature [4]

Among the plants the bitter principles are having the following category:

Iridiod monoterpenes , diterpenes , triterpenes , alkaloids, ketone and amino acids, sesquiterpene lactones, and flavinoids.

GLYCOSIDE [5]

Bitter glycosides are found mainly in the plants of family Gentianaceae. These have the activities like stomachic, febrifuge, digestive etc. These types of glycosides chemically do not belong to same class, but prominent drugs contain glycosides of monoterpene iridoids with pyran cyclopentane ring. These posses lactone ring, and are soluble in water. The bitter-tasting monoterpenoid lactones known as iridoids are also components of volatile oils and have been used to stimulate actions within the body, such as mucosal or gastric secretion. The attachment of glucose to a hydroxyl group on the lactone ring is the determining factor in recognizing a lactone. These isoflavonoid polyphenols are sometimes also referred to as iridoid glycosides, because they are often present in glycosidic form. Iridoids usually occur in angiosperms, especially valerian, gentian, blue flag, and orris root, and can have, aside from the therapeutic actions described above, antimicrobial and antileukemic properties.

Gentopicroside and amrogentin are obtained from the dried fermented rhizomes and root of yellow gentian, gentiana lutea. Gentiopicroside is also known as Gentiopicrin or Gentiamarin. Chemically, it is a seco-iridoid component.[6] It is the principle component of the plant and occurs in the extent of About 2% on hydrolysis it produces gentiogenin and glucose. A biphenolic acid ester of gentiopicroside, amarogentin (0.025-0.050%) has a bitterness value of about 5000 times greater than that of gentiopicroside. In the natural products amarogentin is considered as bittermost substance and impart a bitter taste in even 5.8 lakhs time dilution. Sweroside and swertiamarin are the other bitter obtained from the plant.

FLAVINOIDS[5]

These primarily function as a plant pigment giving color to flower, fruits and foliage. They are widely distributed and abundant throughout the plant world. They all share the same chemical skeleton a central benzene ring joined to a benzo gama pyrone structure. All flavinoids are formed via the shikimic acid and acetate pathway with different degree of oxygenation and hydroxylation determining individual variation.

Flavonoides can be grouped according to structural dieference. Approximately 80% of known flavonoid are classified as flavonoid flavonones and dimmer of these such as bioflavonoids. Other categories of flavonoids includes chalcones, aurones and the glycosyl flavonoids.

Flavonoid are regarded as having anti-inflammatory (inhibit inflammatory metabolites and granulation tissue formation), anti allergic (inhibit histamine release), and anti-oxidant effects. They are well known for strengthening and protective effect on fragile capillary and venous structures. Flavonoid often exhibit their therapeutic function through an ability to inhibit enzyme system (eg lipooxygenase, cyclo-oxygenase, elastase and aldose reductase) as well as free radical scavenging and co-factor activity for the anti-oxidant, vitamin c. Other actions demonstrated by different flavonoids include demonstrated by different flavonoids include hepatoprotective, anti-spasmodic , hypo-cholesterolaemic, diauretic, anti-viraland, anti-bacterial effects. Eg: Quercitrin, quercetin, kaempferol.

DITERPENOIDS

These are C20 compounds derived from four isoprene units and are non-volatilein nature. These C20 natural compounds are biosynthetically prepared from geranyl phosphate. These compounds are rich in families Leguminoseae, Cistraceae, Pinaceae, etc.

TRITERPENOIDS

They are present in free forms or as ester or glycosides and are abundant in nature. These are C30 compounds, biosynthetically prepared from 6 isoprene units. They include aliphatic tetracyclic and pentacyclic compounds. These are commonly present in most of the dicotyldonous plants, belonging to the families Leguminoseae Caryophyllaceae, Apocyanaceae, etc**.**

EXAMPLES

There are various plants in the pharmacognosy field which are significant for human being. some of them are described below[7,8]

1. CINCHONA

BIOLOGICAL SOURCE- It is obtained from the dried bark of the plant *Cinchona calisaya, C. officinalis.* Which are belomging to the family Rubiaceae. The chemical constituent of the cinchona bark are quinine and quinidine. The uses of cinchona bark are in antimalerial and antiarrythmic drugs.

2. GENTIAN

BIOLOGICAL SOURCE- It is obtained from the rhizome and rootpart of the plant *Gentiana lutea* which are belonging to the family Gentianaceae. The active chemical constituent of the plant are gentiopicrin, gentisic acid, gentianose and gentioside. It uses in apetite, heartburn, vomiting and germ killer.

3. CHIRATA

BIOLOGICAL SOURCE- It is obtained from the entire herb of the plant *Swertia chirata*. Which are belonging to the family Gentianaceae. The active chemical constituent of the plant are chiratin, amarogentin, and ophelic acid. It is use in blood pressure ass tincture and infusions.

4. RAUWOLFIA

BIOLOGICAL SOURCE- It is obtained from the dried rhizomes and root of the plant *Rauwolfia serpentiana* which are belonging to the family Apocynaceae. The active chemical constituent of the plant are ophioxylin and reserpine. It is uses in sedation, hypertension, bradycardia and cns depressant.

5. KALMEGH

BIOLOGICAL SOURCE- It is obtained from the dried leaves and tender shoots of the plant *Andrograhis paniculata* belonging to the family Acanthaceae. The active chemical constituent of the plant are andrographolide and kalmeghin. It uses in antihelmintic disease and in cholera.

6. NUXVOMICA

BIOLOGICAL SOURCE- It is obtained from the dried ripe seeds of the plant *Strychnos nuxvomica* belonging to the family Loganiaceae*.* The active chemical constituent of the plant are strychnine and brucine. It uses in erectile dysfunction and anemia.

7. QUASSIA

BIOLOGICAL SOURCE- It is obtained from the dried stem wood of the plant *Picrasma excels* belonging to the family Simarubaceae*.* The active chemical constituent of the plant are Quassin, neoquasssin and picrasmin. It uses in anorexia, constipation and fever.

8. PICRRORHIZA

BIOLOGICAL SOURCE- It is obtained from the dried rhizome of the plant *Picrrorhiza kurrora* belonging to the family Scorphulariaceae. The active chemical constituent of the plant are picrooside-I,II and kutkoside. It uses as cardiac and cerebral tonic, anthelmintic, in paralysis, Epilepsy and gout.

REVIEW OF LITRATUTE

There are various bitter plants which are very significant in the field of pharmacognosy. Some of them are as:

- According to GABRIEL .F IBIKUNLE AND EMMANUEL O. OGBADOYI the Treatment options for trichomoniasis are extremely limited. Newer drugs are therefore needed. Antitrichomonal effects of *G. kola* nuts were evaluated so that extracts with significant antitrichomonal activities can be standardized for use in phytotherapy of trichomoniasis. Powdered nuts were extracted with 100% methanol (A) and 50% methanol (B). The marc from A was further extracted in water to obtain (C). A, B, C, and fractions of A were screened against *Trichomonas gallinarum in vitro*. Antitrichomonal activities were in the order A> B > C at 24 h with LC50 and LC90 of 36.14., 50.12, 212.9 and 293.77, 535.29, 5355.4 (.g/ml) respectively. At 48 h, the order was B> A > C with LC50 and LC90 of 58.51, 139.55, 195.62 and 195.62, 1434.09 and 2887.29 (.g/ml) respectively. It is concluded that these extracts are sufficiently trichomonacidal and therefore potentially useful as therapeutic agents in the control of trichomoniasis[9].

- According to PAULA GARDINER Chamomile is widely used throughout the world. Its primary uses are as a sedative, anxiolytic and antispasmodic, and as a treatment for mild skin irritation and inflammation.Chamomile's main active constituents are chamazulene, apigenin, and bisabolol. Despite its widespread use as a home remedy, relatively few trials have evaluated chamomile's many purported benefits. Randomized controlled studies have shown conflicting results for the treatment of dermatologic and mucosal irritations including eczema and mucositis. Animal trials suggest efficacy as a sedative, anxiolytic and antispasmodic, but clinical studies in humans are needed. Chamomile is generally safe for consumption, although patients with hypersensitivity to ragweed and other family members of the Compositae family should use caution[10].

- According to RAFATULLAH S., TARIQ M. The effect of Swertia chirata has been studied on experimentally induced gastric ulcers in rats. The ethanolic extract of chirata significantly reduced the intensity of gastric mucosal damage induced by indomethacin and necrotizing agents. It produced a significant decrease in gastric secretion in pylorus-ligated rats. The extract inhibited acetylcholine-induced contraction of guinea pig ileum, suggesting its anti-cholinergic activity. Pretreatment of rats with the extract significantly prevented ethanol-induced gastric wall mucus depletion and restored the non-protein sulfhydryl (NP-SH) content in the glandular stomachs. These findings support the use of chirata for the treatment of gastric ulcers in traditional medicine[11].

- According to BJ GURLEY, A SWAIN, The effects of goldenseal (Hydrastis canadensis) and kava kava (Piper methysticum) supplementation on human CYP3A activity were evaluated using midazolam (MDZ) as a phenotypic probe. Sixteen healthy volunteers were randomly assigned to receive either goldenseal or kava kava for 14 days. Each supplementation phase was followed by a 30-day washout period. MDZ (8mg, per os) was administered before and after each phase, and pharmacokinetic parameters were determined using standard non-compartmental methods. Comparisons of pre- and post-supplementation MDZ pharmacokinetic parameters revealed significant inhibition of CYP3A by goldenseal (AUC(0–N), 107.9743.3 vs 175.3774.8 ng . h/ml; Cl/F/kg, 1.2670.59 vs 0.8170.45 l/h/kg; T1/2, 2.0170.42 vs 3.1571.12 h; Cmax, 50.6726.9 vs 71.2750.5 ng/ml). MDZ disposition was not affected by kava kava supplementation. These findings suggest that significant herb–drug interactions may result from the concomitant ingestion of goldenseal and CYP3A substrates[12]. According to P. OVADJE, S. CHATERJEE, the Aqueous DRE effectively induces apoptosis in human leukemia cell lines in a dose and time dependent manner. Very early activation of caspase-8 and the subsequent activation of caspase-3 indicate that DRE may be inducing extrinsic or receptor-mediated apoptosis. Caspase inhibition rendered this extract ineffective, thus DRE-induced apoptosis is caspase-dependent. Moreover, the dominant-negative FADD cells that are unable to form a complete DISC (death-inducing signalling complex) were resistant to DRE treatment, which further confirms our hypothesis that DRE induces receptor-mediated apoptosis. Interestingly, non-cancerous peripheral blood mononuclear cells (PBMCs) exposed to aqueous DRE under the same treatment conditions as leukemia cells were not significantly affected[13].

- According to KHONDOKER DEDAURL ALAM, MOHAMMAD SHAWKAT ALI, the hypoglycemic effect of ethanolic extract of leaf and its different fractions i.e. pet-ether, dichloromethane and methanol fraction of *Swertia chirata* (family-Gentianaceae) on *Swiss albino* mice at fasting condition. Tail tipping method was used as the mean of the investigation. Ethanolic extract of leaf and its pet-ether fraction showed significant hypoglycemic activity by about 32% and 47.2% reduction of

blood glucose level respectively after 3 hours of test sample administration. Dichloromethane and methanol fractions show mild to moderate hypoglycemic effect which is about 14.1% and 15.9% reduction in blood glucose level respectively after 3 hours of drug administration. The test samples were administered at a dose of 250 mg/kg body weight of *Swiss albino* mice. Glibenclamide at a dose of 5 mg/kg body weight was used as standard in this study[14].

- According to A.E. ADEGBITE and E. B. SANYAOLU, the Mitotic studies were carried out on *Allium cepa* (onion) root cells treated with different concentrations of aqueous leaf extract of *Vernonia amygdalina* (bitter leaf). The onion root cells showed reduced mitotic indices with corresponding increase in concentration of the bitter leaf extract [200 g/L (C2), 400 g/L (C3) and 500 g/L (C4)]. Chromosomal aberrations, such as endopolyploidization, lagging of chromosomes and cells with giant chromosomes, were also observed in onion roots treated with same. No chromosomal aberration was observed in the control and in onion roots treated with 100 g/L (C1) of the leaf extract. These observations indicate that abnormal use of this medicinal herb could cause genetic damage. Low concentration and wide spacing of dosage are, therefore, suggested for its dietary intake or use in herbal medicine[15].

- According to SHWETA MISHRA, S.K.TIWARI, ARUN KAKKAR *Andrographis paniculata* (Burm.f.) Nees (Acanthaceae) is a medicinal plant traditionally used for the treatment of cold, fever, laryngitis and several infectious diseases ranging from malaria to dysentery and diarrhoea. The plant is widely used in Ayurvedic and Homeopathic systems of medicines. The medicinal value of this plant is due to the presence of active ingredients *viz* andrographolide and neoandrographolide which are derivatives of diterpenoids. The content of these active ingredients in plant varies with in plant parts and with the geographical distribution. In order to study the variation in andrographolide content, plant material was collected from 15 districts of Madhya Pradesh and evaluated through a simple, quick and accurate HPLC method using C-18 ODS-2 column. The chemoprofiling study showed significant variations in the concentration of active ingredients in the leaves as well as in whole plant. The study also revealed that andrographolide content was maximum in leaves of the accession collected from Seoni (1.82%) followed by Chhindwara (1.48%)[16].
- According to YI-CHIAN WU and CHING-LIANG , the dried root of *Angelica sinensis* (Danggui), is a herb used in Chinese medicine to enrich blood, promote blood circulation and modulate the immune system. It is also used to treat chronic constipation of the elderly and debilitated as well as menstrual disorders. Research has demonstrated that Danggui and its active ingredients, as anti-arthrosclerotic, anti-hypertensive, antioxidant anti-inflammatory agents which would limit platelet aggregation, are effective in reducing the size of cerebral infarction and improving neurological deficit scores[17].

- According to WALBER TOMA, JULIANO DESOUZA GRACIOSO, the plant of *quassia amara* is a source of numerous compounds including both b -carbonile and cantin-6 alkaloids as well as, primarily, the bitter compounds known as quassinoids. We analyzed the possible antiulcerogenic activities of four extracts of different polarities: 70% ethanol (70% EtOH), 100% EtOH, 100% dichloromethane (DCM), and 100% hexane (HEX) obtained from *Quassia amara* bark. All extracts, administered at doses of 5000 mg/kg orally and 1000 mg/kg intraperitoneally, caused neither toxicity or death. In the indomethacin/bethanechol-induced gastric ulcer, 70% EtOH, 100% EtOH, DCM and HEX extracts, 100 mg/kg, *p.o*., inhibited the gastric ulcer (22.5, 23.4, 50.5, 46.8%, respectively).70% EtOH, 100% EtOH, DCM, and HEX extracts reduced the gastric injury induced by the hypothermic restraint–stress test in mice (70.7, 80, 60, 82.7%, respectively). In the pylorus

ligature of the mouse stomach, following pre-treatment with a single intraduodenal administration of 100 mg/kg of each extract, only 70% EtOH did not change the biochemical parameters of gastric juice. 100% EtOH, DCM and HEX extracts presented decreased gastric juice content, increased pH values and decreased acid output. We also determined the antiulcerogenic activity on HCl–EtOH-induced gastric ulcers in mice at four doses (25, 50, 75, 100 mg/kg, *p.o*.), then evaluated the possible dose-dependent relation and calculated the ED50 values. Except for 70% EtOH at a dose of 25 mg/kg, the other extracts showed significantly activity (*p*,0.05). The free mucous amount in the gastric stomach content was also evaluated. All extracts showed significant increases (*p*,0.05) of free mucous. This effect was abolished when the animals were pre-treated with indomethacin. Prostaglandin synthesis was evaluated by the administration of HEX extracts by the oral route (100 mg/kg). Prostaglandin synthesis was significantly, increased by 52.3% (*p*,0.05), and this effect was abolished with prior administration of indomethacin. We concluded that *Quassia amara* is a probable source for a new drug to treat gastric ulcers, and the mechanism of its activity relates to cytoprotective factors, such as mucous and prostaglandins, but there is still the possibility that antisecretory activity is involved in its antiulcerogenic effect[18].

- According to SASIKUMAR, J.M., MAHESHU, V., SMILIN, A.G., the potential of Common *Nilgiri Barberry* (*Berberis tinctoria* Lesch.) fruits as nutraceutical/functional food, polyphenolic contents and the *in vitro* antioxidant and antihemolytic activity were determined. The phenolic content (TP) of the fresh fruits is 410 ± 0.082 mg gallic acid equivalents (GAE)/100g and total flavonoid content (TF) is 320 ± 0.120 mg quercetin equivalents (QE)/100g. The methanol extract exhibited scavenging capacity towards 1, 1 – diphenyl – 2- picryl hydrozyl (DPPH·), superoxide anion, hydroxyl ion radicals and nitric oxide. The TEAC of fruit extract ranged from 1.063-2.364 mM TE/g. The extract also exerted strong reducing capacity and had strong Fe3+ chelation (EC50 45.24 ±1.42 µg mL-1), and remarkable reduction of erythrocyte hemolysis (EC50 71.1 ± 0.22 µg ml-1). Positive correlations were observed between polyphenolic contents and the antioxidant capacities. In conclusion, the Barberry fruit from India, endowed with polyphenols, could be a potential source of for the development of natural antioxidants/nutraceuticals[19].

- According to M. MOHAMADI, A. M. MASKOOKI., The quality and shelf life of foods of containing lipids (fats and oils) significantly reduce due to rancidity. Applications of natural antioxidants are one of the most effective manners to prevent the oxidation of oils and lipids. The antioxidant properties of juice extracted from barberry fruit (*Berberris vulgaris*.L) using maceration and SWE (10 bars and 120 - 180°C) methods were investigated and compared with conventional method. The amount of phenolic compound and reduction power of all samples were determined and the data were statistically analyzed using multifactor design. The results showed that the total amount of phenolic compound increased with increasing of pressure and temprature from 1861.9 to 2439.1 (mg Gallic acid /100gr Dry matter). The ability of reduction power of SWE obtained antioxidant extract compared with BHA (synthetic antioxidant) and ascorbic acid (natural antioxidant). There were significant differences among reduction power of extracts and there were remarkable difference with BHA and Ascorbic acid ($P<0.01$)[20].

- According to S. GNANAVEL, R. BHARTIDASAN, The antimicrobial effect of some selected Indian medicinal plants *Strychnos nux-vomica* and *Cassia angustifolia,* were selected. The solvents used for the extraction of plant leaves were n-butanol, methanol and distilled water. The invitro antimicrobial activity was performed by agar well diffusion method. The most susceptible gram-positive bacteria were *Staphylococcus and Salmonella* while other most susceptible gram negative bacteria was *klebsiella pneumonia* and fungal species namely *Aspergillus terreus, Aspergillus flavus*

and Aspergillus niger. The n-butanol extract of plant *Strychnos nux-vomica and Cassia angustifolia,* inhibit all the bacterial and fungal strains investigated. The most active extract was compared with the standard antibiotics, penicillin, streptomycin and ampicillin with 100mg disc. In the present study *Strychnos nuxvoimica* and *Cassia angustifolia* showed maximum inhibition against the fungal and bacterial organisms tested. Thus the n-butanol plant extracts could be used to control the above microbes[21].

- According to G. LEELAPRAKASH, J.CAROLINE ROSE, the *in vitro* antimicrobial and antioxidant activity of aqueous and methanol extracts of *Momordica charantia* leaves. In preliminary phytochemical analysis we observed glycosides, alkaloids, phytosterols, saponins, phenolic compounds, proteins, fats and fixed oils and flavonoids, and thin layer chromatography was also performed. Antimicrobial activity was evaluated for *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae* and *Bacillus subtilis* by using stokes disc diffusion and well diffusion methods. Methanolic plant extract showed a maximum zone of inhibition in *E.coli* by disc method but in well diffusion method *Bacilli* and *Klebsiella* showed maximum inhibitory activity. The antioxidant activity of the plant extract was also determined by DPPH and ABTS methods using ascorbic acid and gallic acid as standards respectively. IC50 values were also calculated[22].

- According to KHOSROKHAVAR R, AHMADINI A, The pA2 values for antihistaminic activity of methanolic extract and dexchlorpheniramine were calculated (extract; pA2± S.E.M = 3.53 ± 0.16 [-logC(g/l)]; dexchlorpheniramine; pA2 ± S.E.M.= 9.36 ± 0.14 ([-logC (M)]) and compared with each other. The pA2 values of anticholinergic activity of methanolic extract and atropine were also calculated (extract; pA2± S.E.M = 4.18 ± 0.17 [-logC(g/□)]; atropine, PA2 +S.E.M = 8.99 ± 0.13 [-logC(M)]) and compared. The results indicated antihistaminic and anticholinergic activity of methanolic extract[23].

- According to BAKARE R. I., MAGBAGBEOLA O. A., The aqueous extract of the plant showed inhibitory activity against castor oil induced diarrhoea. A significant reduction ($p< 0.05$) in the gastrointestinal motility in charcoal meal test in rats was observed. The extract decreased volume of intestinal secretion induced by castor oil with a significant effect ($p< 0.05$) on the gastric emptying of the test animals compared to control rats. Inhibition of the gastrointestinal propulsion and fluid secretion by the extract suggest the extract might exert its antidiarrhoeal activity by antisecretory mechanism[24].

CONCLUSION AND RECOMMENDATION

A deep study of bitters may reveal many facts facilitating the study diabetes and some CNS related diseases like anxiety and epilepsy. Some of the drugs used as anti-diabetic also show bitter properties. Many studies have been performed to identify pharmacologically activity with a limited toxicity. In this context, ethno pharmacology represents the most important way possible of finding interesting and therapeutically helpful molecules. It can be useful also in various manufacturing industries as raw material. Though the bitter drug plant is in high demand in traditional ayurvedic formulation and pharmaceutical industry it is recommended that there should be proper package of practice of cultivation and collection of bitter plants. Thus, numerous medicinal and ethno botanical uses of nearly all parts of the plant indicate a long association of the plant with people, especially in India Considering these facts it may be hypothesized that bitters may have some relation in mechanism with that of anti-anxiety drugs and these have considerable effect on Diseased condition.

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