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A Safe Approach in Remedial Hepatoprotective Treatment Using Phytomedicines

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Abstract

The usage of herbal medicines has been traced back to China for more than 5,000 years. Similar to this, India's Ayurvedic medical system, which dates back more than 5,000 years, still heavily relies on herbal remedies. Between 75 to 80 percent of the world's population, mostly in underdeveloped nations, still relies heavily on herbal medicine for primary healthcare. This is primarily due to the widespread misconception that herbal medications are safe, inexpensive, and readily available. The World Health Organization (WHO) estimates that the usage of herbal treatments is two to three times greater than the use of conventional medications worldwide.

Keywords – Ayurvedic medical system, Herbal medicines, Conventional medications worldwide

Introduction

In the majority of the nations where ethnomedicine is frequently used to treat cut wounds, skin infections, swelling, aging, mental illness, cancer, asthma, diabetes, jaundice, scabies, eczema, venereal diseases, snakebite, and gastric ulcers, tribal healers teach the local population how to make herbal medicines. They don't retain any documents, and the majority of the information is passed down orally from one generation to the next. The World Health Organization (WHO) has expressed a strong interest in gathering information about the medicinal plant use by indigenous peoples around the globe. A lot of developing nations have stepped up their efforts to record the ethnomedical information on therapeutic plants. The hunt for scientific support for claims made by tribal healers regarding Indian plants has become more intense. People will be better informed about effective pharmacological treatment and improved health status after these regional ethnomedical formulations have undergone thorough scientific evaluation and dissemination. The demand for herbal medications is currently high, and their acceptance is growing daily. 800 plants have been

employed in indigenous medical systems, and approximately 500 plants with therapeutic uses are documented in ancient literature.

India is home to a sizable collection of medicinal plants that are applied in conventional medical procedures. Many plant species are used by the various indigenous medical systems, including Siddha, Ayurveda, Unani, and allopathy, to treat various illnesses. Because of the toxicity and side effects of allopathic treatments, the use of herbal medicine is growing in popularity. This caused a dramatic rise in the number of companies making natural drugs. Since ancient times, herbal remedies have served as the primary treatment in traditional systems of medicine. The techniques are still used today due to their biological advantages as well as their status in many cultures around the world and their significant contribution to preserving human health. 6 More than 500 traditional groups use roughly 800 plant species to treat various diseases in India, despite the fact that more than 20,000 medicinal plant species have recently been discovered there. Because it has no side effects, plant-derived medication is currently the first line of primary healthcare for 80% of the world's population.

A significant portion of pharmaceutical prescriptions in the United States currently contain at least one component derived from plants. A total of 121 medicinal items were developed in the last century using traditional knowledge that was gathered from various sources. Due to its effectiveness, safety, and lack of negative side effects, herbal medications are also much sought after for use in primary healthcare in the developed world. Also, they provide treatments for age-related illnesses including memory loss, osteoporosis, immunological problems, etc. for which there is no modern therapy. When synthetic acetyl salicylic acid (aspirin) was first made available to the public in 1897 by Friedrich Bayer & Co., the long-standing connection between plants and human health started to break down. Aspirin was separately found as a treatment for aches and fevers by inhabitants of both the New and the Old worlds. Aspirin is a safer synthetic analogue of salicylic acid, the active component of willow bark.

Herbal medicine refers to the use of plants, plant parts, their water or solvent extracts, essential oils, gums, resins, exudates, or other types of advanced products made from plant parts for therapeutic purposes, or, in a more traditional medical sense, to treat, cure, or prevent a disease in animals or people.

There are currently 121 active chemicals derived from plants that are used in medications prescribed around the world. 11% of the 252 medications that the World Health Organization (WHO) considers to be basic and essential come completely from plants, while a sizable portion are synthetic medications made from natural precursors. Digoxin from Digitalis spp., quinine and quinidine from Cinchona spp., vincristine and vinblastine from Catharanthus roseus, atropine from Atropa belladonna, and morphine and codeine from Papaver somniferum are a few examples of significant medications made from plants. India has a long, colorful, and varied cultural past. The concept of health and healing plays a significant role in this culture and tradition.

Hence, across all ethnic communities and varied ecosystems, there is a vast knowledge base relating to health and healing. This knowledge foundation, which is dismissive of regional health traditions, has been diluted over the last few decades due to rising mainstream cultural influences. Effective recording and assessment programs must be immediately implemented in order to revive regional health customs; else, this magnificent people's health culture would be lost forever. This nation is aptly referred to be the botanical paradise of the world and may be the largest producer of therapeutic herbs. Few commercially significant therapeutic herbs can be found outside of this country.

Almost 3000 plants are officially recognized as having therapeutic use in India. Around 6000 plants are reportedly used in India for traditional, folk, and herbal medicine, which accounts for about 75% of the medical requirements of Third World nations. In India, there are thought to be about 7800 manufacturing facilities for pharmaceuticals, and it is thought that each year, they use over 2,000 tons of herbs. Allium sativum, Aloe arbedensis, and Panax species preparations—three of the ten herbal medications that sell the best in affluent nations—are available in India. Over 7000 businesses produce traditional medicines, either standardized or not.

Literature Review

Rajiv P et al(2017) .'s study, Screening for Phytochemicals and FTIR Analysis of Myristica dactyloids Fruit Extracts, revealed that, when compared to other solvent extracts, methanolic extract contained the highest concentrations of alkaloids, steroids, flavonoids, phenolic compounds, proteins, carbohydrates, cardio glycosides, and saponins. According to FT-IR analysis, the fruit extracts include a variety of functional groups, including carboxylic acids, aromatics, alkanes, alcohols, phenols, aliphatic amines, alkenes, and amine groups.

Evaluation of Acute Oral Toxicity of Synergistic Formulation Extract of Traditional Contraceptive Herbs was the subject of research by Kadam AB et al. (2017). 2000mg/kg of a high extract was provided as a single dosage, and the effects on mortality, behavioral pattern, and spontaneous locomotor activity were assessed. The upper limit of 2000 mg/kg did not result in any fatalities. The results indicated that both aqueous and petroleum ether had LD50 values more than 2000 mg/kg. Hence, plant synergistic extract is safe.

The effects of natural products on fructose-induced nonalcoholic fatty liver disease (NAFLD) were explored by Qian Chen et al. in 2017. Fructose is a common sugar addition in processed foods and beverages. Consuming too much fructose can result in dyslipidemia and hepatic steatosis, which can both lead to the onset of metabolic syndrome. According to recent studies, fructose-induced non-alcoholic fatty liver disease (NAFLD) is linked to a number of pathological processes, including those that increase lipogenesis, cause mitochondrial dysfunction, activate inflammatory pathways, and result in insulin resistance.

Pharmacological Significance of Withania Coagulans in Health and Diseases was reported by Neelam B. Bare et al. in 2017. The shrub's berries are employed in the coagulation of milk. Moreover, they are used to treat various intestinal infections, flatulent colic, and dyspepsia. Withania coagulans (Stocks) Dunal is used to cure impotence, wasting illnesses, impotence in children, and nervous weariness. Asthma, biliousness, and liver ailments are treated using its fruits. specifically, withanolide extracted from plants is thought to have The plant has been found to have antimicrobial, anti-inflammatory, anti-tumor, hepatoprotective, anti-hyperglycemic, cardiovascular, immunosuppressive, free radical scavenging, antimutagenic, and central nervous system depressant properties.

Withania Coagulans was the subject of research by Avinash Shankar et al. (2016) in the management of diabetes mellitus. Oral administration of withania coagulans fruit extract in the early morning and late at night as an adjuvant with ongoing anti-diabetic medications in older patients and with OHA in new cases gradually established normoglycemic level both fasting and pp and spared the dose of ongoing anti-diabetic medication and patients taking insulin became totally free of insulin prick. Also, it improved diabetic complications, bioregulated lipid profiles, lowered the dosage of OHA, and did so without affecting hemato, hepatic, or renal function.

HPTLC fingerprint analysis and antibacterial activity of Cassia fistula L. leaf extracts were reported by Chavan RT et al. in 2016. Alkaloids, sugars, glycosides, saponins, triterpenes,

tannins, flavonoids, photobatalin, and anthracene were found in the methanol and aqueous leaf extracts according to the phytochemical screening. The presence of flavonoids (Peak 4) and alkaloids was confirmed by the HPTLC analysis of methanolic extract of leaves (Peak 3).

Impact of Chloroform Fraction of Withania coagulans Bud on the Regulation of GLUT4 and PPAR -Expression Levels in Diabetes L6 Myotubes was the subject of research done by Sandhiya V et al. in 2016. The chloroform fraction (CF) of a crude medication exhibits 510 g/ml of free radical scavenging activity. The MTT assay's IC50 value was discovered to be 84.7 g/ml. The GLUT4 study demonstrates considerable glucose absorption. Using standard Pioglitazone, PPAR gamma activity modulation of glucose disposal and insulin sensitivity is demonstrated in the skeletal muscles. Withania coagulants' bud holds promise as a treatment for further illnesses.

The primary phytoconstituents of 25 traditional medicinal plants were identified in Nandagoapalan V et al(2016) .'s study on the phytochemical analysis of several traditional medicinal plants in order to correlate their presence with the plants' bioactivities. Standard screening techniques were used on the plants, and the presence of tannins, flavonoids, phenolics, saponins, steroids, cardiac glycosides, and alkaloids were discovered. Alkaloids were found in 16 out of 25 plants, while flavonoids were found in 19 out of 25 plants. These phytochemicals' existence and these plants' potential as medicines can be linked.

In 2016, Salem Mohamed Edrah et al. published Qualitative and Quantitative Analysis of Phytochemicals of Different Extract for Ephedra Altissima from Libya. Terpenoids and anthraquinones, which are absent from some crude extracts, as well as the chemical constituents (Qualitative and Quantities analysis) most commonly found in plant crude extracts (tannins, saponins, flavonoids, cardiac glycosides, and alkaloids), which were formerly steroids, were taken into account.

Preliminary phytochemical, acute oral toxicity, and anticonvulsant activity of Brassica juncea seed extract were proposed by Nguyen Le Bao Duy et al. (2016). The phytochemical analysis revealed the presence of alkaloids, flavonoids, saponins, tannins, terpenoids, and phenolic compounds in B. juncea seeds. The extract was found to be safe and non-toxic to mice up to 5000 mg/kg body weight, according to the Acute Oral Toxicity testing.

Objective of the study

The study's goals include validating acute oral toxicity, researching rat behavioral coordination, investigating the effects of progesterone on obesity in rodents, investigating the effects of fructose on hyperlipidemia in rodents, and investigating the analgesic action.

Research Methodology

According to the physical characteristics of the crude medication to be extracted, which may be liquid or solid, extraction is described as the process of isolating material from an insoluble residue that may be liquid or solid by treatment with a solvent. Withania coagulans Dunal flower buds were gathered, and the dried material was ground into a coarse powder that was used for further research and ethanol extraction using a Soxhlet device.

Extract of ethanol

Marc was extracted using 2.5 liters of ethanol after being dried from the petroleum ether extract. For the next 24 hours, the extraction was continued. After the extraction process was finished, the extract was filtered, and the solvent was eliminated using distillation at a low pressure. The residue produced was brown. It was then kept in a desiccator. The extracts were employed for pharmacological research as well as phytochemical screening to identify components.

Data Analysis and interpretation

Table showing Preliminary Phytochemical Studies

S.No	Plant Constituents	Test / reagent	Ethanolic extract of *Withania coagulans*
1.	Steroids	Salkovaski Liberman Burchard Test	+
2.	Alkaloids	Dragendroff's Hager's test Mayer's test Wagner's test	+
3.	Saponin	Forms test Haemolysis test	-
4.	Fat and oils	Filter paper test	-
5.	Tanins and phenolic compounds	Ferric chloride test Lead acetate test Pot. Dichromate Bromine water	-
6.	Flavonoids	Shinoda test Lead acetate test	+
7.	Carbohydrates	Molisch test Fehling's test Barfoed's test	+
8.	Proteins	Millons test Biuret test Xanthoprotein test	+
9.	Amnio acid test	Ninhydrine test	+
10.	Glycosides	Legal's test Baljet test Bontrager's test Keller Kiliani test	+

Table showing IR Spectral Data of the Ethanolic extract of Withania coagulans

S. No	Wavenumber (cm^{-1})	Interpretation
1.	3418.82 & 3382.21	Polymeric association of alcohols and phenols indicates presence of miscellaneous chromophoric groups
2.	2974.21	Chromophoric hydrocarbon - Alkene
3.	2934.88	Chromophoric hydrocarbon - Alkene
4.	2112.11	Alkene monosubstituted
5.	1722.28	Saturated 6-membered and higher ring
6.	1662.94	α, β - unsaturated bending- acyclic
7.	1575.63	C-NO_2 aromatic nitro compounds
8.	1414.44	Phenolic OH bending
9.	1215.63	Aliphatic CN vibrations
10.	1049.29	Aromatic C-C multiple bond stretching
11.	925.15	CH bending; Alkene monosubstituted
12.	879.63	One Hydrogen atom bending
13.	814.00	Two adjacent hydrocarbon atoms
14.	777.55	C-X stretching
15.	648.58	C-X stretching
16.	621.68	C-H stretching

Table showing Effect of Ethanolic extract of Withania coagulans on Head dips in Albino rats

S. No	Groups	Total time spent with the head dips		No. of head dips in the holes			
		Before Treatment	After Treatment	30 min	60 min	90 min	120 min
1	**Control** (Normal Saline 5mL/kg, b.w., *p.o.*)	67 ± 6.87	67 ± 7.58	15 ± 2.85	19 ± 0.49	13 ± 0.24	16 ± 0.92
2	**Standard** (Diazepam 1mg/kg, b.w., *i.p.*)	62 ± 6.17	179 ± 27.57	34 ± 1.84	34 ± 0.28	35 ± 0.92	39 ± 0.37
3	**Test** Ethanolic Extract of *Withania coagulans* (200mg/kg, *p.o.*)	66 ± 6.52	155 ± 11.71***	32 ± 0.9**	29 ± 0.98**	30 ± 0.47**	34 ± 0.74**

n = 6 Values are expressed as ± S.E.M. Values are Mean ± SEM (n=6) two way ANOVA. Where, *** P<0.001, ** P<0.01 and * P<0.05

Prior to the ethanolic extraction, the plant was pulverized and defatted using petroleum ether. The flower buds of Withania coagulans Dunal were gathered, dried, and extracted using ethanol. 60% of the ethanolic extract is produced. Infrared spectroscopy was used to determine whether the ethanolic extract of Withania coagulans Dunal's flower buds contained any potential functional groups. The Withania coagulans Dunal flower buds' ethanolic extract revealed potential stretching and bending that indicates the presence of the functional group.

Conclusion

In fructose-induced hyperlipidemic rats, the ethanolic extract of Withania coagulans at a dose of 200 mg/kg demonstrated considerable hypolipidemic action. This can be seen in the group that received treatment with 200 mg/kg of the ethanolic extract of Withania coagulans, which resulted in a decrease in blood lipid markers such triglycerides, total cholesterol, LDL, VLDL, SGOT, and SGPT and an increase in HDL content. It is discovered that the serum glucose has decreased significantly. When the Tail Flick Analgesic test was performed using the ethanolic extract of Withania coagulans, a substantial inhibitory effect was observed. When Pheritima posthuma was exposed to the ethanolic extract of Withania coagulans, it had

a substantial inhibitory impact at higher doses of 75 mg and 100 mg of normal saline. In an antibacterial test, Withania coagulans' ethanolic extract significantly inhibited growth of both gram-positive and gram-negative bacteria as well as fungi. Future research may shed light on the functional groups in the Withania coagulans ethanolic extract that are responsible for the behavioral coordination, anti-obesity, anti-hyperlipidemic, analgesic, anthelmintic, and antimicrobial effects, as well as help to elucidate the precise mechanism of action that underlies the observed significant activity with low toxicity and a higher therapeutic index.

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