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Toxicity profile of traditional herbal medicine

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ABSTRACT

Medicines obtained from natural sources have become the basis for pharmaceutical drugs. Traditional herbal medicines are naturally occurring plant derived substances; these have been used for treatment and cure of various diseases and as a nutraceuticals. Toxicological research and testing help to live safely and predict benefit from synthetic and natural substance while avoiding harm. The toxicity study is done for data profiling and safety of the herbal drugs, the toxicity study of various plant and herbal formulation are reported. This review briefly discusses the need of toxicity study, toxicity produced by plants and safe traditional herbal medicine.

Keywords: Toxicity, Medicinal Plant, Herbal Formulations, Toxic constituents.

INTRODUCTION

The natural wealth of India includes many herbs having medicinal property. There are several literatures shows that India has been using traditional medicines since ancient times. Three major traditional systems exist in India using medicinal plants are Ayurveda, Unani and Siddha. There is a common thread running through these system is their fundamental principal and practices. Indian materia medica incudes about 2000 drugs of natural origin which are derived from different traditional system and traditional practice [1]. Medicinal plants have considerable potential to supplement incomes and improve livelihood for rural population. But there are serious issue that needs to be collection, processing and marketing [2]. Toxicology is the study of how chemical substances affect the normal processes and interact with living system. The uses of this information provide safe exposure levels. Toxicological research and testing help to live safely and predict benefit from synthetic and natural substance while avoiding harm. All chemicals can cause harm at some dose level of exposure. That means exposure to a specific small amount of any substance will have no detectable effect on normal biological process and is considered safe. Some doses have beneficial effects but increasing exposure will, at some point cause harmful effect and substance considered toxic at that level [3]. All herbs should be tested individually before including it in research regarding its toxicity. Toxicity testing is conducted to get information on the biological activity and mechanism of action of the drug. The information generated by the test is used in hazard identification and risk management of the drugs. Preclinical studies of herbal drugs provide scientific justification for their traditional use and prove that they are safe and efficacious [4].

Need of herbal toxicity testing

The concern related to toxicity testing of drugs is for safety purposes. All drugs included in the research must be devoid of any toxicity [5]. Because herbs are classified as a dietary supplements not food or drugs; that why they do not have to go through the pre-market testing that drugs and food additives do. Acute toxicity testing is conducted to get information regarding its safety and further evaluate biological activity and mechanism of action of the drug. The information generated by the test is used in hazard identification and risk management of the drugs [6]. In medicinal plants found one or more than one biological activity and plants have been used traditionally in the various herbal formulation. Table-1 listed various plants, plant parts, type of extract and medicinal uses whose toxicity profile have been reported and found to be safe. These plants have been used in different pharmaceutical and commeracial formulations. Toxicological evaluation of herbal drug extract is shown in Figure-1.

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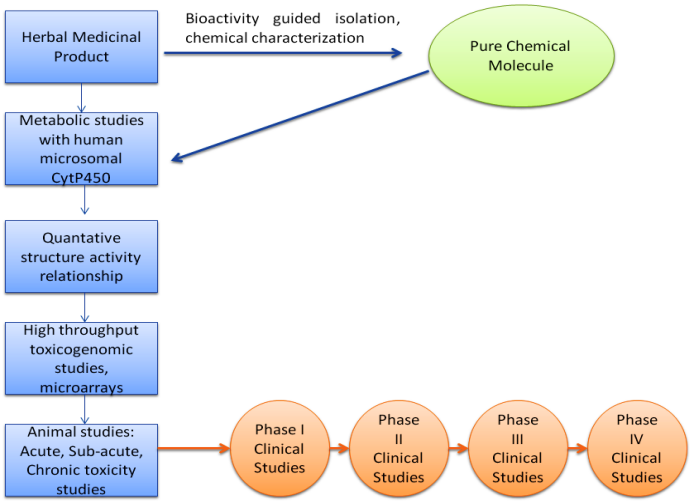

Figure 1: Toxicological evaluation of herbal extract

Toxicity of Herbs

Inspite of increased demand of herbs in market for its use in different medicnal products still there are several issues related with their safety. Very less (< 10 %) marketed herbal products are standardized and strictly followed quality control measures [7]. Very little information is available regarding the toxicity of these products. Some plants produce toxic constitutents for defence purposes. These are *Aconitum columbianum, Blighia sapida, Trifolium hybridum, Digitalis purpurea, Gymnocladius dioica, Hyoscyamus niger, Solanum nigrum, Sanguinaria Canadensis, Atropa belladonna, Physostigma venenosum, Pteridium aquilinum* and *Podophyllum peltatum,* these toxic substances are not distinguished from therapeutically active ingredients. There certain phytochemicals alkaloids, flavonoids, terpenoids and saponins which can mimick or antagonize the functions of signalling molecules, neuropeptided, hormones and neuropeptides in humans [8-11]. Terpenes have inhibitory cholinesterase activity [12] however some terpenes act on specific receptor like GABA etc [13]. Saponins contain phytochemicals having potent antimicrobial properties and it also acts as surfactants [14]. Several heavy metals are also present in herbs like lead, cadmium, mercury and arsenic there may also responsible for toxicity of plants [15-16].

Safety and efficacy of herbals

It is one of the most essential and demanding tasks for scientists working in herbal drug development to investigate the efficacy of herbal medicine, to scrutinize adverse effects, to identify marker compounds or therapeutic agents in medicinal or botanical and to serious contaminants from herbal mixtures. Most importants resons or causes of botanical or herbal drug toxicity are improper identification or authentication of Botanical or herbals, improper or mislabeling of plant material, contamination of herbals with microorganisms, contamination of herbals with fungal toxins such as aflatoxin, contamination of herbals with pesticides and heavy metals, interaction with conventional drugs upon concomitant intake, improper or unprofessional processing and inadequate standardization.

Demand for herbal medicines increases daily in Indian as well as international market that is why the main concern of herbs is not only use but their safety too. Survey says only 10% of herbals in global market are standardized with special reference to marker or active principles and their quality control parameters. Majority of the herbals or plant derived natural products which were use by the majority of population's needs strict development of standardization and quality control parameters. Most of these of plants are far away from its safety data or having very little information regarding their toxicity [17]. This issues lift up concern on their safety and efficacy of herbal drugs. For avoiding potential harmful effects, toxicity testing can reveals some hazards that may be associated with the safer use of herbs or herbal drugs.

Table 1: Toxicity Tested Traditional Medicinal Plants

S.No.	Plant name	Plant parts	Extract	Use	Reference
1.	*Nigella damascena*	Seed	Methanolic	Amenorrhoea diuretic	[18]
2.	*Pisonia Aculeata LINN.*	Leaves	Methanolic	Hepatoprotective and Antioxidant	[19]
3.	*Hemodya(Cassia siamea Lam, le flamboyant, Garcinia cowa Rox)*		Aqueous	Sickle cells	[20]
4.	*Cosmos Caudatus*	Leaf	Ethanolic	Anti-aging agent	[21]
5.	*Astercantha longifolia*	Seed	Ethanolic	Gout and rheumatoid arthritis	[22]
6.	*Crinum giganteum*		Aqueous	Anti-inflammatory	[23]
7.	*Solanum nigrum*	Whole plant	Ethanolic	Pain, fever, inflammation	[24]
8.	*Dalbergia latifolia*	Root	Ethanolic	Muscle relaxant, for diabetes	[25]
9.	*Chrozophora plicata*	Leaf	Chloroform	Tantircuse and jaundice	[26]
10.	*Momordica dioica*	Fruit	Aqueous	Hepatoprotective, antibacterial	[27]
11.	*Boerharia diffusa*	Whole	Methanolic	Headache, anxiety	[28]
12.	*Garuga pinnata*	Leaf	Alcoholic	Diabetes	[29]
13.	*Albizia lebbeck*	Leaf	Methanolic	for snake poison	[30]
14.	*Tephrosia purpurea*		Ethanolic	BronchitIS, diuretic	[31]
15.	*Saccharum spontaneum Linn.*	Root	Ethanolic	Antioxidant, antimicrobial	[32]

16.	*Lygodium flexuosum*	Whole plant	n-hexane	Hepatoprotective	[33]
17.	*Pterospermum acerifolium*	Leaf	methanolic	Analgesic, antioxidant, antiulcer	[34]
18.	*Eupatorium*	Leaf	Methanolic	Antifungal, antimicrobial	[35]
19.	*Eichhornia crassipes*	leaves and shoot		Antimicrobial	[36]
20.	*Combretum Molle*	Leaf	Aqueous	Antibacterial, antifungle	[37]
21.	*Moringa oleifera*	Leave	Ethanolic	Anti inflammatory	[38]
22.	*Carica papaya Linn*	Leaf	Ethanolic	Analgesic, amebicide, antibiotic	[39]
23.	*Annona senegalensis*	Root bark	-----	-----	[40]
24.	*Anacyclus pyrethrum*	Root	Ethanolic	Antibacterial, antidepressant	[41]
25.	*Acalypha indica Linn*		Ethanolic		[42]
26.	*Cyperus rotundus*	Fruit	Water	antidiarrhoeal, antispasmodic	[43]
27.	*Murraya Paniculata*	Leaves	Ethanolic	Stimulant astringent	[44]
28.	*Crinum defixum*	Bulbs	Ethyl acetate, chloroform and ethanol	Pimples, body swelling, dropsy, carbuncles	[45]
29.	*Aconitum laciniatum and Abrus precatorius*	Root Seed	-----	Heart stimulant antifertility and anticancer	[46]
30.	*Cassia auriculata*	Leaf	Ethanolic	Heptoprotective, antioxidant	[47]
31.	*Desmodium gyrans*	Leaf	Ethanolic	Antidote, cardiac-tonic	[48]
32.	*Pistacia integerrima*	Bark	Methanolic	Antioxidant, Antidepressant	[49]
33.	*Shorea robusta*	Leaf	Ethanolic	Analgesic, Anti-inflammatory	[50]
34.	*Anogeissus acuminata*	Leaf	Methanolic	Antidiabetic	[51]
35.	*Datura alba*	-----	-----	Asthma	[52]
36.	*Ziziphus jujuba*	Leaf	Water	Anti-diarrhoeal	[53]
37.	*Ziziphus Xylopyrus*	Stem bark	Chloroform and methanolic	Antidepressant, antimicrobial	[54]
38.	*Curcuma caesia*	Rhizome	Ethanolic	Leprosy, asthma	[55]
39.	*Melia azedarach*	Leaf	Ethanolic	Antiviral, antifertility	[56]
40.	*Citrullus colocynthis*	Root	Chroloform, ethanolic, water	Antimicrobial, antimalarial	[57]
41.	*Momordica dioica*	Seed	Methanolic, aqueous	Asthma , leprosy	[58]
42.	*Bauhinia vahlii*	Whole	Chloroform, ethanolic	Antidiabetic	[59]
43.	*Bauhinia variegate*	Leaf/bark/seed		Antioxidant	[60]
44.	*Rauwolfia serpentina*	Root	Methanolic	Blood pressure	[61]
45.	*Adina cordifolia*	Leaf	Acetone, aqueous	Antifertility, anti-inflammatory	[62]
46.	*Ficus bengalensis*	Bark	Alcoholic	Pain	[63]
47.	*Cassia tora*	Leaf	Methanolic	Skin disease	[64]
48.	*Pongamia pinnata*	Seeds & sprouts		Ulcers, liver pain	[65]

49.	*Plectranthus amboinicus*	Leaf	Methanolic	Antibacterial, antimalarial	[66]
50.	*Piliostigma thonningii*	Leaf		Skin disease	[67]
51.	*Phyllanthus amarus*	Aerial	Juice	Anti bacterial, Antifungal	[68]
52.	*Leucas aspera*	Aerial	Ethanolic	Anti-fungal, anti-microbial	[69]
53.	*Entada pursaetha,Toddalia aculeata, and Ziziphus mauritiana*	Seed, stem, fruit	Ethanolic	Arthritis	[70]
54.	*Coccinia indica*	Root	Aqueous	Skin diseases, ulcer	[71]
55.	*Clerodendron infortunatum*	Leaf	Methanolic	Asthma, fever, burning sensation	[72]
56.	*Capparis zeylanica*	Root	Chloroform		[73]
57.	*C. maxima*	Aerial	Methanolic	Antidiabetic, antitumor	[74]
58.	*Acanthus montanus*	Leaf	Aqueous	-----	[75]
59.	*Bauhinia Variegata Linn*	Root	Ethanolic, aqueous	Antimicrobial, anti-inflammatory, hepatoprotective	[76]
60.	*Cassia occidentalis L.*	Stem, leaf	Hydroalcoholic	Analgesic, febrifuge, diuretic	[77]
61.	*Mucuna pruriens*	Whole plant	Ethanolic	Dysmenorrhoea, amenorrhoea	[78]
62.	*Ageratum conyzoides linn*	Leaf	Methanolic, chloroform	Diuretic, antipyretic	[79]
63.	*Barleria prionitis*	Root	Aqueous	-----	[80]
64.	*Abutilon indicum*	Leaf		Laxative, diuretic	[81]
65.	*Nyctanthes arbor tristis and Maharasnadi ghan*		Methanolic	Antidote for venom	[82]
66.	*Rubia cordifolia linn.*	Root	Methanolic	Gastrointestinal, cardiovascular	[83]
67.	*Semecarpus anacardium*	Nut	Ethanolic	Anti-arthritis, antioxidant	[84]
68.	*Pistacia vera*	Leaf	Ethanolic	Analgesic, carminative	[85]
69.	*Mallotus philippensis*	Leaf	Methanolic	Antifungal, antimicrobial	[86]
70.	*Lawsonia inermis*	Root	Aqueous		[87]
71.	*Calotropis gigantea*	Root	Methanolic	Immunomodulatory, hepatoprotective	[88]
72.	*Eugenia jambolana*	Fruit		Antioxidant,anti-inflammatory	[89]
73.	*Clitoria ternatia*	Root	Methanolic	Antidiarrheal, antihistaminic	[90]
74.	*Alangium lamarckii*	Root	Ethanolic	Anti-inflammatory	[91]
75.	*Boswellia serrata*		n-hexane	anti-inflammatory	[92]
76.	*Tinospora cordifolia*	whole	Decoction	Antidiabetic, antiathritic	[93]
77.	*Cassia fistula*	Seed	Methanolic	Skin diseases, fever	[94]

78.	*Tamarindus indica*	Stem bark	Ethanolic	Dysentery, jaundice	[95]
79.	*Cuscuta reflexa*	Whole	Chloroform, ethanolic	Antitumor	[96]
80.	*Madhuca latifolia*	Seed		Leprosy, peptic ulcer	[97]
81.	*Gloriosa superba*	Root	Aqueous	Blood pressure	[98]
82.	*Phyllanthus niruri*	Leaf	Aqueous	Skin diseases	[99]
83.	*Albizzia odoratissima*	Bark	Methanolic	Skin disease, rheumatism	[100]
84.	*Aristolichia indica*	Aerial	Alcoholic	Antibacterial, antioxidant	[101]
85.	*Curcuma amada*	Rhizome	Ethanolic, chloroform, petroleum ether, acetone	Skin disease	[102]
86.	*Hemidesmus indicus*	Leaf	Ethanolic	Leucorrhoea, bronchitis	[103]
87.	*Terminalia Arjuna*	Leaf	Methanolic	Antipyretic, astringent	[104]
88.	*Capparis aphylla*		Ethanolic	Antidiarrhoea, dysentery	[105]
89.	*Terminalia chebula*	Fruit	Water	Laxative, carminative	[106]
90.	*Alstonia scholaris*	Bark	Aqueous	Fevers, abdominal disorders	[107]
91.	*Cocos nucifera*	Leaf	Chloroform, methanolic	Nourishing hair	[108]
92.	*Ficus glomarata*	Fruit	Chloroform, acetone, ethanolic	Anti-inflammatory	[109]
93.	*Ficus religiosa*	Latex	Methanolic	Antidiabetic, anthelminthic	[110]
94.	*Sphenocentrum jollyanum*	Root	Ethanolic	Anti-inflammatory, anti-angiogenic	[111]
95.	*Ocimum sanctum*	-----	-----	-----	[112]
96.	*Caesalpinia bonducella*	Leaf	Ethyl acetate	Antipyretic, antidiuretic	[113]
97.	*Centella asiatica*	Leaf	Ethanolic	Anti-ulcer, antioxidant	[114]
98.	*Cleome viscosa*	Seed	Ethanolic, aqueous	Antidiarrheal, hepatoprotective	[115]
99.	*Curcuma aromatic*	Leaf	Methanolic	Antimicrobial	[116]
100.	*Colocasia Esculenta*	Leaf	Ethanolic		[117]
101.	*Bacopa monnieri*	Aerial	Ethanolic	Epilepsy, insomnia	[118]
102.	*Oxalis corniculata linn*	Whole plant	Methanolic	Ageing, cancer	[119]
103.	*Smilax zeylanica*	Root and rhizomes	Methanolic	Epilepsy, leprosy	[120]
104.	*Acacia catechu*	Heartwood powder	-----	Anodyne, astringent, bactericide	[121]
105.	*Celastrus paniculatus*	Seed	Alcoholic	Anti-inflammatory, analgesic	[122]
106.	*Tectona grandis*	Bark	Ethanolic	Antiulcer, antimicrobial	[123]

107.	*Zizyphus rugosa*	Root bark	Chloroform, methanolic	Anti-inflammatory, Analgesic	[124]
108.	*Calotropis gigantea*	Root bark	Ethanolic	Antifertility, alexipharmic	[125]
109.	*Peristrophe bicalyculata*	Leaf, stem	Aqueous, butanolic, methanolic	Anti-inflammatory	[126
110.	*Strychnos nox-vomica*	Seed		Rheumatic pain	[127]
111.	*Butea frondosa*	Leaf	Ether, chloroform, Ethanol	Dysentery, piles, ulcers, tumors	[128]
112.	*Andropogon Muricatus*	Root	Ethanolic	Analgesic, antipyretic and anti-inflammatory	[129]
113.	*Azadirachta indica*	Leaf	Aqueous	Skin disease	[130]
114.	*Dioscorea oppositifolia*	Tuber	Methanolic	Fever, diarrhoea leprosy	[131]
115.	*Diospyros melonoxylon*	Leaf	Chloroform, ethanol, petroleum ether	Diarrhoea dyspepsia	[132]
116.	*Atlantia monophylla*	Leaf	Ethanolic	Digestive trouble, antioxidant	[133]
117.	*Ficus racemosa*	Bark	Alcoholic, aqueous	Antipyretic, anti-inflammatory	[134]
118.	*Andrographis paniculata*	Isolated material	-----	Antipyretic, analgesic	[135]
119.	*Cardiospermun helicacabum*	Stem	Chloroform, methanolic	Diuretic, stomach ache	[136]
120.	*Cassia Occidentalis*	Bean	-----	Constipation, diabetes, oedema	[137]
121.	*Phyllanthus emblica*	Fruit	Aqueous	Jaundice, cough	[138]
122.	*Indigofera tinctoria*	Leaf	Ethanolic	Jaundice, gout	[139]
123.	*Dalbergia sissoo*	Bark	Ethanolic	Anti-inflammatory, analgesic	[140]
124.	*Mitragyna parvifolia*	Leaf	Ethanolic	Muscular pain, burning sensation	[141]
125.	*Dioscorea bulbifera*	Tuber	Aqueous	Antidyslipidemic	[142]
126.	*Cucumis prophetarum*	Fruit	Alcoholic	Anti-inflammatory	[143]
127.	*Phyllanthus Amarus*	whole	Aqueous	Antibacterial, antiviral	[144]
128.	*Peperomia pellucida*	Leaf	Ethanolic	Fever, abdominal pains	[145]
129.	*Smilax zeylanica linn*	Roots and rhizomes	Ethanolic	Antidiabetic, antioxidant	[146]
130.	*Hemidesmus indicus*	Stem	-----	Antiulcer, diuretic	[147]
131.	*Tecomella undulata*	Bark	Methanolic	Gonorrhoea, leucoderma	[148]
132.	*Pongamia glabra*	Leaf	Ethanolic	Anti-inflammatory, analgesic	[149]
133.	*Portulaca oleracea*		Methanolic	Anti-inflammatory, Antifungal	[150]
134.	*Strychnos potatrum*	Seed	Aqueous	Water purifier	[151]

135.	*Terminalia belerica*	Fruit	Ethanolic	Chronic diarrhea, dysentery	[152]
136.	*Vitex negundo*	Leaf	Ethanolic	Anti-inflammatory, anticonvulsant	[153]
137.	*Boerhavia diffusa*	Leaf	Aqueous	Heart disease, night blindness	[154]
138.	*Argemone mexicana*	Whole	Aqueous	Anti-anthelmintic, anti-inflammatory	[155]
139.	*Calotropis procera*	Root barks	Aqueous and hydroalcoholic	Hydrophobia	[156]
140.	*Albizia amara*	Bark	Ethanolic	Inflammations	[157]
141.	*Tamarindus indica*	Leaf	Ethanolic	Anti-inflammatory, antimicrobial	[158]
142.	*Spathodea campanulata*	Leaf	Ethanolic	Hypoglycaemic, antioxidant	[159]
143.	*Fagara heitzii*	Stem and barks	Aqueous	Analgesic	[160]
144.	*Catharanthus roseus*	Leaf	Methanolic	Antioxidant, antidiabetic	[161]
145.	*Sphaeranthus indicus Linn*	Whole plant	Ethanolic	Jaundice, hepatopathy and gastropathy	[162]
146.	*Annona squamosa*	Leaf	Aqueous	Anti-tumor, anti- diabetic and antilipidaemic	[163]

CONCLUSION

This review paper describes the need of toxicity study of herbal plant and herbal formulation. The provided infomation may be helpful in further study of herbal plant or formulation and practising herbs for different traditional systems of medicine. It is necessary to conduct research to support the therapeutic claim and also insure the herbal plant and herbal formulation are safe for the human consumption.

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CONFLICTS OF INTEREST

No conflicts of interest.

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