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A review on phytotoxins and qualitative tests for their detection

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Abstract
Plants and their products have been used in diets, therapeutics, hunting, fishing, war and killing living beings. Bioactive molecules are responsible for both medicinal as well as poisonous nature of a plant. Dose or quantity explores whether a plant is poisonous or not and it also determines the extent of toxicity produced by the plants. Toxic principles which are synthesised by the plants as a defence system can produce adverse effects in the consumer by various mechanisms. The important phytotoxins include cyanogenic glycosides, cardiac glycosides, toxic alkaloids, toxalbumins, saponins, resins, tannins etc. Livestock with fodder scarcity and access to the poisonous plants are at high risk of poisoning. This paper provides brief information regarding various phytotoxic principles highlighting their sources, toxicological effects and qualitative detection tests.

Keywords: Poisonous plants, phytotoxins, toxic principles, cyanogenic glycosides, toxalbumins, qualitative tests

Introduction
Herbal medicines are widely used in therapeutics and believed to be safe having no side effects. However, plants as medicine either possess side effects or are ineffective because an effective drug is always having one or other side effects [1]. According to Paracelsus, all things are poison and nothing is without poison; solely the dose determines that a thing is not a poison [2]. In fact, salt, water or even oxygen in excess can prove fatal [1]. Plants and their products have been used not only as food and medicines but also for hunting, fishing, war, assassination and malicious killing of animals [2, 3]. Phytoconstituents include primary and secondary plant metabolites which are responsible for the positive and/or negative health effects exhibited by the plant [4]. Poisonous plants have the potential to cause severe toxicities, injury or even death in man and animals after accidental consumption, inhalation, dermal or ocular exposure [3]. In general, plant poisoning is more extensive in animals including pets and livestock in comparison with human beings [5]. In context with the livestock industry, plant toxicosis results in severe economic losses in terms of high mortality, chronic illness, emaciation, reduced weight gain, reproductive disorders, photosensitization and other conditions [6]. Nevertheless, toxic plants have the unpleasant test, offensive odour and less palatability hence usually are avoided by the animals, however, fodder scarcity or certain conditions make animals to consume these plants [7]. The concentration of toxin in the plant determines the severity of toxicosis, which is dependent on certain factors including plant part, age/stage of the plant, sunlight and soil type where the plant has grown in [2].
As far as safety is concerned, plants can be classified into three categories. Firstly, the plants with toxic principles at therapeutic doses which are to be used only with the advice of qualified clinician. For example, plants like *Digitalis* spp., *Areca catechu*, *Atropa belladonna*, etc. Next class includes plants with potential pharmacological properties which are safer under appropriate circumstances. Lastly, the plants which are known to be potentially toxic like *Lantana camara*, *Strychnos nuxvomica* and others [1, 8]. Toxic plants have a worldwide distribution and are further categorised into two classes. One type represents plants having toxic principle and known to cause poisoning while other group include apparently non-toxic plants which are poisonous only under certain conditions [6].

Plant toxins
Toxins are special poisonous substances that are produced in small quantity by biological systems such as plants (phytotoxins), animals (zootoxins), fungi (mycotoxins) or bacteria (bacteriotoxins) [2, 6]. The important phytotoxins include cyanogenic glycosides (linamarine, amygildin), cardiac glycosides (digitalis, nerin), alkaloids (strychnine, atropine, nicotine), toxalbumins (ricin, abrin), triterpenes (lantadene), saponins, resins, tannins, etc. [9, 10, 29].

The toxic principles are the adoption of plants to prevent themselves from being consumed by predators and ultimately promoting their survival [2, 3]. Phytotoxins in the animal or human body, act through various specific mechanisms involving receptors, transporters, enzymes and even genetic material at specific cells and tissues to produce toxic effects [10]. The general mechanisms of plant poisoning include teratogenicity, ribosomal inactivation, cytotoxicity, neurotoxicity, cardiotoxicity, hepatotoxicity, nephrotoxicity, thyrotoxicosis, photosensitization, protease inhibition, haemagglutination, vitamin antagonism and metal chelation [9-11]. It has been reported that some of the plant products especially mucilages, polysaccharides and tannins interfere with the biological effects of active principles [1]. An overview of some of the important plant toxins with their sources and effects is presented in table 1.

Determination of Plant Toxins

To establish clinical use of an herbal product its toxicological evaluation is crucial including screening for toxic constituents [12]. Similarly, diagnosis of poisoning due to plants also requires determination of toxic principle. In this regard, two types of tests are present for the determination of plant toxins i.e. presumptive and confirmatory tests [13]. The reliminary tests determine phytotoxins qualitatively (whether present or not) or sometimes semi-quantitatively (based on the time required for the onset of reaction and/or intensity of development of colour etc.) [14]. The confirmation of presumptive tests can be done by modern techniques viz. liquid chromatography-mass spectrometry, gas chromatography-mass spectrometry, high-performance liquid chromatography, fourier transform infrared spectroscopy etc. which act through separation and identification of individual molecule. However, these confirmatory tests are more expensive, time-consuming and require various equipment which are not available or affordable in all circumstances [4, 13]. Therefore, the qualitative tests which are simple, fast and economic play a crucial role in presumptive investigation and field analysis of large number of samples [13, 14]. Various qualitative tests for presumptive detection of some of the important phytotoxins have been mentioned in table 2. The successful determination of a toxic principle in a plant material largely depends on the extraction procedure. Amongst various methods of phytotoxin extraction, the classical Stas-otto's method (Figure 1) and its modification is considered as the best method [15, 16].

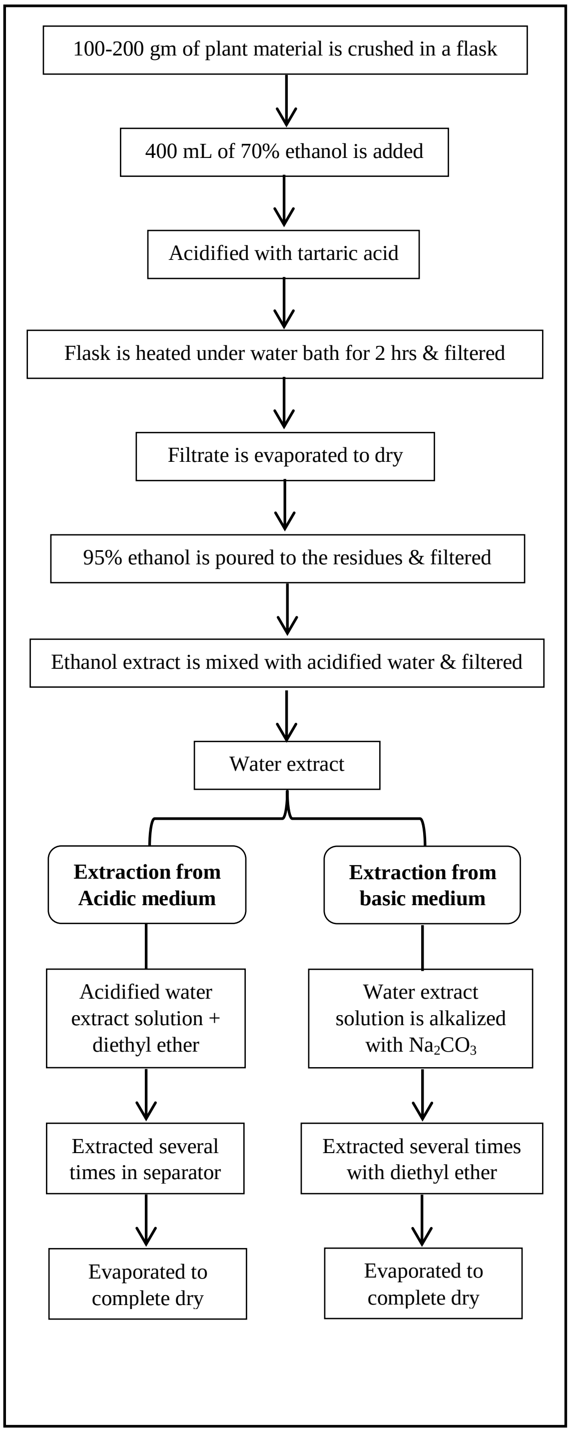

Fig 1: Stas-otto's method for extraction of Phytotoxins from plant materials [16].

Table 1: Sources and toxicological effects of various plant toxins

Phytochemical Class	Toxic Principle(s)	Sources: Botanical and common name(s)	Toxic Part(s)	Principle Toxicological Effects	Citations
Cyanogenic glycosides	Linamarine	*Linum usitatisismum* (Linseed)	Seeds	Inactivation of Cytochrome oxidase results in reduction in oxygen utilization by cells which ultimately leads to cell death due to cytotoxic anoxia	[6, 7, 17, 18]
	Dhurrin	*Sorghum vulgare* & other spp.	Leaves		
	Amyglidin	*Amygdalus communis* (Almond)	Seeds		
	Lotusin	*Lotus* spp. (Bird's-foot trefoil)	Leaves		
	Sinigrin	*Sinipis alba* & *S. nigra* (Mustard)	Seeds		
Cardiac glycosides	Nerioside, oleandroside, oleandrin, nerin, folinerin, digitoxigenin	*Nerium oleander* (Oleander), *N. indica* (Kaner)	All parts	Cardiotoxic action through inhibition of Na^+/K^+-ATPase pump leading to cardiac arrhythmia, conduction block, bradycardia, loss of contractility, asystole & cardiac arrest	[6, 7, 8, 19]
	Calotroxin, calactin, gigantin, uscharin	*Calotropis procera; C. gigantean* (Ruchki)	All parts		
	Digitalis	*Digitalis purpuria* & other spp.	Leaves		
Glucosinolate	Progoitrin	*Brassica* spp. (Cabbage)	Leaves	Yields goitrogen thiocyanate	[8
Alkaloids	Atropine, Hyoscine, Hyoscyamine Daturine	*Atropa belladonna* (Deadly nightshade), *Datura* spp. (Dhatura), *Hyocyamus niger* & related plants	All parts (seeds↑)	Anticholinergic manifestations like xerostomia, dysphagia, mydriasis, tachypnoea, tachycardia etc.	6, 8, 20]
	Strychnine	*Strychnos nux vomica* (Kuchla)	Seeds	Antagonism of inhibitory neurotransmitter glycine which results in CNS stimulation	[6, 7, 21]
	Nicotine	*Nicotiana* spp. (Tobacco); *Lobelia* spp. (Indian tobacco)	All parts	Initial stimulation followed by depression of nicotinic receptor in autonomic ganglia	[7, 8]
	Sanguinarine	*Argemone Mexicana* (Firangi dhatura)	Seeds	Dropsy, cardiomyopathy & glaucoma	[2, 8]
Steroidal alkaloids	Cyclopamine	*Veratrum alba* & other spp.	All parts	Teratogenic (sheep↑) and causes cyclops, anopthalmia & microophalmia	[8, 9]
Glycoalkaloids	Solanine	*Solanum tuberosum* (Potato)	Flowers, Sprouts, Tubers	GIT irritation, haemolysis, CNS stimulation followed by depression	[5, 22, 23]
Non protein amino acids	Mimosine	*Leucaena leucocephala* (Subabool), *Mimosa pudica* (Sensitive plant)	Leaves↑	Disease condition: Jumbey/Lamtoro Yields goitrogen which inhibit thyroxin synthesis and results into alopecia, anestrum, failure of conception, lameness & oral ulcers	[8, 24]
Toxalbumins (Lectins)	Ricin	*Ricinus communis* (Castor bean)	All parts (seeds↑)	Act as ribosome inactivating proteins (RIPs) & inhibit protein synthesis resulting in severe cytotoxic effects in various organs	[6, 13]
	Abrin	*Abrus precatorius* (Rathi)	Seeds		
	Jatrophin	*Jatropha curcas* (Ratanjyot)	Seeds & fruits	Drastic purgation & haemorrhagic gastroenteritis	[5, 27]
Triterpenes	Lantadene	*Lantana camara* (Panjphuli)	Leaves & berries	Causes hepatotoxicity, cholestasis and secondary photosensitization	[6, 7, 8]
Secquiterpines	Parthenin	*Parthenium hystrophorus* (Gajar ghaas)	Leaves↑	Produces allergic contact dermatitis, primary photosensitization & liver damage	[7, 8]
Furanoterpenes	–	*Ipomoea batatus* (Sweeet potato)	Tuber	Pneumotoxicity, pulmonary oedema & dyspnoea	[8]
Polyphenolic compounds	Gossypol	*Gossypium* spp. (Cotton)	Seeds	Protein binding & iron chelation rendering digestion & utilization respectively; inhibition of various enzymes.	[6, 8]
Saponins	–	*Ipomoea caenea* (Beshram)	Leaves	Haemolysis, anaemia, haematuria, liver damage	[8]
	–	*Tribulus terrestris*		liver damage & Secondary photosensitization	[8]
Resins	Tetrahydo-cannabinol	*Cannabis sativa* (Marijuana)	All parts (leaves↑)	Stimulation of dopamine pathway in brain resulting in hyper excitability followed by depression and other signs	[2, 6]
	Scammonin	*Ipomea orizabensis* (Jalapin)	Root & bark	Severe GIT irritation leading to drastic purgation (cathartic action)	[6]
	Turpethin	*Ipomea turpethum* (Indian jalap); *I. hederaceae*			
Tannins	Gallotannin	*Quercus* spp. (Oak)	Leaves, bark, nuts	Denaturation of cell proteins with anorexia, depression and gastro-enteric signs	[6, 7]
Phytates	–	*Sesamum indica* (Til)	Seeds	Inhibition of calcium absorption from gut	[8]
Anthraquinones	*Not reported*	*Cassia fasciculate* (Senna) *C. occidentalis*	Seeds	Strong binding with cell membrane & muscle degeneration	[6]
Phytoestrogens	Coumestans, isoflavones	*Glucine max* (Soybean); *Medicago sativa* (Alfalfa, lucern); *Trifolium repens* (white clover)	Various parts	Reversible infertility, prolongation of oestrus & oestrogenic effects	[8, 23]
Coumarin	–	*Melilotus alba; M. officinalis* (Sweet clover)	All parts	Yields antithrombin dicoumarol leading to anticoagulant action & bleeding disorder	[5, 8]
Other	Nitrates and Nitrites	*Medico sativa* (Alfalfa); *Zea mays* (Maize); *Sorghum* spp.; *Brassica* spp.;	Various parts	Nitrates combine with haemoglobin to form methaemoglobin resulting in reduced oxygen	[5, 7, 8], [25, 26]

		Avena sativa (Oats); *Amaranthus retroflexus* (Pigweed) *Beta vulgaris* (Sugar beet)		carrying capacity hence tissue hypoxia/anoxia. Nitrite ions causes vasodilation leading to vasogenic shock	
	Oxalates and Oxalic acid	*Halogeton glomeratus; Oxalis pescaprae* (Soursob); *Sarcobatus vermiculatus* (Grease wood); *Rheum rhaponticum* (Rhubarb); *Anagallis arvensis* (Nile phuli); *Beta vulgaris* (Sugar beet); *Amaranthus retroflexus* (Pigweed)	Various parts	Ca^{++} chelation causes hypocalcaemia & results into reduced muscular activity, altered nerve transmission, impairs blood clotting & cell functioning; Blockage of renal tubules leads to nephrosis; crystallization in brain causes neuronal damage leading to nervous signs	[5, 6, 8, 28, 21]
	N-Propyl disulphide	*Allium cepa* (Onion); *A. ampeloprasum* (Garlic)	All parts	Inhibition of erythrocyte glucose-6-phosphate dehydrogenase leading to haemolysis and haemolytic anaemia	[6, 8]
	Thiaminase	*Pteridium aquilinium* (Bracken fern)	All parts	Destroys thiamine and causes its deficiency	[7, 8]
	Aplastic anaemia factor			Aplastic anaemia, thrombocytopenia resulting into haemorrhagic syndrome	

Table 2: Chemical analysis for detection of some plant toxins [14, 16, 17, 30, 31]

Name of the Test(s)	Methodology	Observations for Positive Reaction
Detection Hydrocyanic acid/Prussic acid		
Test 1	Step 1: 20mL aqueous mercuric chloride + 10mL aqueous methyl orange solution + 2mL glycerine + filter paper strips are dipped + dried Step 2: Plant extract in a test tube + dried filter paper strips are held at the mouth of test tube	Paper turns pink colour in 2 min.
Test 2	15mL distilled water + 1mL cupric acetate + 5mL glacial acetic acid + filter paper is dipped + wet filter is then dipped in the sample	A blue colour in 10 sec.
Scheerer's test (Picrate paper)	Step 1: Saturated solution of picric acid + filter paper strips are dipped + dried + soaked in 10% NaOH solution + dried at room temperature Step 2: Small amount of plant sample in wide mouthed test tube + tartaric acid + filter paper is fixed in the neck of test tube + sealed (heated if required)	The paper turns pink to brick red
Picrate paper test	Step 1: Filter paper strips are dipped into 0.5% picric acid and then in 5% Na_2CO_3 + dried Step 2: Picrate paper is suspended over the crushed plant material in vial ($CHCl_3$ is added if required) + fixed using stopper (+ warmed if required)	The paper turns orange to red from yellow (*Disappearance of colour after addition of a drop of 10% acetic acid to the paper indicates false positive test*)
Feigl-Anger paper test	Step 1: Pieces of filter paper are dipped in the solution mixture[a] + dried Step 2: The paper is suspended over the crushed plant material in test tube/vial + fixed using cork/stopper	The paper turns bright blue or purple from pale blue-green
Silver nitrate test	A drop of silver nitrate is placed on microscope slide; it is inverted over the mouth of flask containing extract + heated gently	A white turbidity which shows needle-like crystals microscopically
Detection of Atropine		
Vitali's test	Moisten extract + Fuming nitric acid, evaporate to dryness, cool + few drops of 5% alcoholic potassium hydroxide	A violet colour, turn red and finally becomes colourless
Gerrard's test	Plant extract + 2 drops of 2% mercuric chloride (in 50% alcohol) solution	A red colour [atropine]; a yellow colour turns red on heating [hyoscyamine]
Auric chloride test	Extract solution + auric chloride	A citron yellow precipitate
Detection of Caffeine		
Test 1	Extract + nitric acid + 33% ammonium hydroxide	Violet colour turns red [caffeine/theobromine/ theophylline]
Mayer's reagent test	Few mL filtrate + 1-2 drops of Mayer's reagent[b] (along the sides of test tube)	Caffeine does not form precipitate while other alkaloids do
Detection of Morphine		
Test 1	Few drops of extract sol. + 2mL of warm iodic acid, shaken + equal volume of chloroform, shaken well and allowed to stand (+ dil. Ammonium hydroxide)	Brown colour which get deepened by addition of Ammonium hydroxide [morphine]
Neutral ferric chloride test	Extract + few drops of 5% neutral ferric chloride sol.	Blue colour [morphine]; Red colour changing to black [apomorphine]; no colour [codein/heroin]
Marquis's test	Extract + few drops of mixture (3mL conc. H_2SO_4 + 3 drops of formalin)	A purple-red colour changing gradually to violet then blue [morphine]; A violet colour (not initially purple-red) changing blue [codein, apomorphin]
Husemann's test	Extract + 2-3 drops of 3mL conc. H_2SO_4, heated on water bath for an hour, allowed cooling + 1-2 drops of HNO_3 OR a crystal of potassium nitrate	A reddish violet colour turns to blood-red and then to reddish yellow and finally disappear [morphine]
Detection of Nicotine		
Test 1	10mg extract + 1 drop of formalin + conc. HNO_3	A rose colour

Test 2	Extract sol. + chlorine water	A red-brown precipitate
Detection of Digitalis		
Test 1	Extract + few drops of mixture (equal parts of conc. H_2SO_4 + alcohol) + a drop of dil. ferric chloride solution	A yellow-brown solution turn bluish-green by $FeCl_3$ solution [digitalin]
Bromine water test	Extract + conc. H_2SO_4 + Bromine water	Green not decolorized [digitoxin]; orange-yellow rapidly changing to blood-red turning cherry/violet [digitalin]; red, intensified with bromine [digitonin]; emerald green turning brown [stophanthin]
Detection of Strychnine		
Test 1	Dissolve extract in conc. H_2SO_4 + crystal of potassium dichromate; shake gently	A coloured streamers of blue, violet, red & orange playing around crystals
Test 2	Extract + pinch of solid manganese dioxide + 1mL conc. H_2SO_4	A violet colour
Test 3	1mL extract solution + 1mL 1% tannic acid	A white precipitate
Test 4	1mL extract solution + 0.5mL dil. Tincture of iodine	Decolourization and precipitation of Tr. Iodine
Test 5	1mL extract + few drops of 0.1% potassium permanganate solution	Decolourization of $KMnO_4$
Mandelin's test	2 drops of 1% ammonium vanadate solution + extract solution + few drops of 30% Ammonium hydroxide solution	Blue changing to brilliant violet; Ammonium hydroxide turns it to brilliant reddish violet
Detection of Ergot		
Test 1	Plant extract[c] + dissolved in few mL of glacial acetic acid + $FeCl_3$ solution + allowed to float cautiously on conc. H_2SO_4 in test tube	A brilliant violet/intense blue colour at the junction
Test 2	Ether extract is used for following three tests: (i) Extract + potassium hydroxide + heated	Fishy odour
	(ii) Extract + Aqueous sodium hydroxide	A red colour
	(iii) Extract + conc. H_2SO_4	Orange turns blue at junction
Detection of Nitrates/Nitrites		
Joint test 1	1% diphenylamine (in conc. H_2SO_4) + equal amount of sample	A blue colour [nitrate / nitite]
Joint test 2	Step 1 : Sample + dil. H_2SO_4 Step 2: Sample + conc. H_2SO_4	Brown fumes with dilute and/or conc. H_2SO_4 [nitite]; brown fumes only with conc. acid but not with dilute acid [nitrate]
Grie's test	2mL Grie's reagent[d] + unknown solution drop by drop	A red colour [nitite]
Indole test	A drop of sample in test tube + 10 drops of 0.015% indole solution (in ethanol) + 5 drops of conc. H_2SO_4	A red colour [nitite]
Test for nitrite	2 drops of test solution on a slide +2 drops of 1% sulphanilamide solution (in 1.5N HCl) + 2 drops of 0.02% N-1-naphthyl-ethylene diamine dihydrochloride solution (in absolute alcohol)	A pink colour [nitite]
Test for nitrate	1mL test sample + 1-4 drops of salicylic acid	A yellow colour [nitrate]

[ ] = Denotes presence of the specific plant toxin.
a = 1gm of each chemicals (4,4' tetramethyldiaminodiphenylmethane; *N,N*-dimethylanilinein & copper ethylacetoacetate) is dissolved in 100mL $CHCl_3$ to prepare three different solutions. Working solution: Equal volumes of each of the solutions are mixed together.
b = Mayer's reagent (Solution A: 1.358gm mercuric chloride + 60mL distilled water; Solution B: 5gm potassium iodide + 10mL distilled water; Working solution: solution A + solution B + distilled water to make final volume 100mL).
c = Plant material treated with acidified alcohol to obtain the red coloured extract.
d = Grie's reagent (Solution I: 1gm sulphanilic acid + 75mL distilled water + 25mL glacial acetic acid; Solution II: 3gm α-naphthalamine + 70mL distilled water + boil + filter + 30mL glacial acetic acid + allow solution to turn pink after decomposition; Working solution: solution I + solution II in 1:1 ratio).

Conclusion

Plants are natural sources of medicines and are assumed to be safe but they may prove potentially poisonous due to presence of some toxic compounds. Qualitative tests for detection of plant toxins are very useful for presumptive diagnosis and mass screening of plant samples, as they are inexpensive, easy and rapid. Performing a test is always easier than its interpretation, the latter requires expertise and experience. The negative reaction does not rule out the possibility of presence of a toxic compound (false-negative test). Similarly, a positive test always is not a definite proof of occurrence of a toxic constituent in the sample (false-positive test). Therefore, it is advised that multiple tests should be performed for each toxin and the chemical test should be combined with biological, botanical and other tests to ensure correct interpretation.

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