IJPSR (2015), Vol. 6, Issue 7 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 28 October 2014; received in revised form, 27 January, 2015; accepted, 28 February, 2015; published 01 July, 2015

MEDICINAL PLANTS - FROM TRADITIONAL USE TO TOXICITY ASSESSMENT: A REVIEW

S. Chanda [1]*, J. Parekh [1], Y. Vaghasiya [1], R. Dave [1], Y. Baravalia [2] and R. Nair [1]

Phytochemical, Pharmacological and Microbiological Laboratory [1], Department of Biosciences, (UGC-CAS), Department of Biochemistry [2], Saurashtra University, Rajkot-360005, Gujarat, India

Keywords:

Acute toxicity, Chronic toxicity, Hematological parameters, serum biochemical parameters, Gross behaviour

Correspondence to Author:
S. Chanda

Department of Biosciences, (UGC-CAS), Saurashtra University, Rajkot-360 005, Gujarat, India

E-mail: svchanda@gmail.com

ABSTRACT: Herbal medicine is gaining popularity once again and there is an increased interest in green medicine simply because it is considered as safe. Traditionally also plants and plant extracts were used to cure many diseases and disorders. However, before usage it is of utmost important to ensure its safety. The extract may be therapeutically very efficient but if it's toxicity assessment is not worked out, it will not be accepted. Hence, toxicity assessment of plants with proven therapeutic use is of utmost important. Toxicity data are required to predict the safety associated before the use of medical products. In the present review, parameters required to be analyzed in acute, sub acute and chronic toxicity are discussed with their relevant importance. In the end ninty eight plants whose toxicity is worked out are listed along with their botanical name, family, ethnomedicinal uses, part used, solvent used, safety levels, dose levels used, route of administration, LD_{50} values and references. Researchers who wish to work on some pharmacological activity can directly choose one of these plants since their toxicity assessment is already done.

INTRODUCTION: Medicinal plants from time immemorial have been used in virtually all cultures as a source of medicine [1]. They are considered to be the backbone of traditional medicine and are widely used to treat acute and chronic diseases. The World Health Organization estimated that perhaps eighty percent of the inhabitants of the world rely chiefly on traditional medicines. It, therefore, approved the use of herbal products for national policies and drug regulatory measures in order to strengthen research and evaluation of the safety and efficacy of herbal products.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.6(7).2652-70

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.6(7).2652-70

The report has suggested that of the 119 plant derived drug listed by WHO study, 74% were discovered as a result of chemical studies to isolate the active compounds responsible for the use of original plant in traditional medicine [2]. The use of plants for healing purpose is getting increasingly popular as they are believed to be beneficial and free of side effects.

However, the rationale for the utilization of medicinal plants has rested largely on long-term clinical experience with little or no scientific data on their efficacy and safety [3]. Medicinal herbs have their use as medicament based simply on a traditional folk use that has been perpetuated along several generations. With the upsurge in the use of herbal medicines a thorough scientific investigation of these plants is imperative, based on the need to validate their folkloric usage [4]. Herbs are supposed to be safe but many unsafe and fatal side effects

have been reported [5, 6]. These could be direct toxic effects, allergic reactions, effects from contaminants and/or interactions with drugs and other herbs [7]. Phytotherapeutic products are many times, mistakenly regarded as less toxic because they are 'natural' [8]. Nevertheless, those products contain bioactive principles with potential to cause adverse effects [9].

An adverse effect is defined as an abnormal, undesirable or harmful change following exposure to the potentially toxic substance. The ultimate adverse effect is death but less severe adverse effects may include altered food consumption, altered body and organ weights, visible pathological changes or simply altered enzyme levels [10]. Thus, all the "natural" products used in therapeutics must be submitted to efficacy and safety test by the same methods used for new synthetics drugs [11].

Toxicology is the fundamental science of poisons. A poison is generally considered to be any substance that can cause severe injury or death as a result of a physicochemical interaction with living tissue. However, all substances are potential poisons since all of them can cause injury or death following excessive exposure. On the other hand, all chemicals can be used safely if exposure of people or susceptible organisms to chemicals is kept below defined tolerable limits [10]. Appropriate dose of a drug should be determined by preliminary studies of acute toxicity. Such studies are essential to prevent any overdose of drug which may interfere with results of experiment.

The lethal dose (LD_{50}) is defined as the dosage of a substance which kills 50 per cent of the animals in a particular group, usually determined in an acute, single exposure study. There are three major sites for the absorption of foreign compounds: the skin, lungs and gastrointestinal tract. The gastrointestinal tract is the most important in toxicology as most foreign compounds are ingested orally.

The lungs are clearly important for all airborne compounds whereas the skin is only rarely a significant site for absorption [12]. They are also helpful in understanding toxicity profiles of the drug [13]. The multiple dose study with a drug is also necessary. But, in order to choose the doses to be used in the study, the clinical observation of the acute assay is important along with pharmacological activity studies in animals and in humans [14, 15]. Daily clinical observation is of major importance as well as the final observation [16]. The doses to be evaluated in chronic toxicity in animals must be larger than that suggested for use in humans [17].

Toxicological studies help to decide whether a new drug should be adopted for clinical use or not [18]. Depending on the duration of exposure of animals to drug, toxicological studies may be of three types viz. acute, sub-acute and chronic [19]. Toxicity depends not only on the dose of the substance but also on the toxic properties of the substance. The relationship between these two factors is important in the assessment of therapeutic dosage in pharmacology and herbalism [20].

For clinical trials designed to study pharmacologic effects of candidate products, more extensive preclinical safety data would be needed to support the safety of such studies. The critical preclinical information required includes a two week toxicology study in sensitive species (usually rodents) plus toxicokinetics that should allow determination of the no observed adverse effect level (NOAEL). For some compounds and types of toxic effect there will clearly be a dose below which no effect or response is measurable. There is thus a threshold dose. The concept of a threshold dose for the toxic effect is an important one in toxicology because it implies that there is a NOAEL. The NOAEL is usually based on animal toxicity studies. The NOAEL is important for setting exposure limits. For example, the acceptable daily intake (ADI) is based on the NOAEL. This is a factor used to determine the safe intake for food additives and contaminants such as pesticides and residues of veterinary drugs and, hence, to establish the safe level in food [12].

Acute toxicity:

Acute toxicity is defined as the toxic effects produced by single exposure of drugs by any route for a short period of time [21]. Acute toxicity studies in animals are considered necessary for any pharmaceutical intended for human use. The main

objective of acute toxicity studies is to identify a single dose causing major adverse effects or life threatening toxicity, which often involves an estimation of the minimum dose causing lethality. The studies are usually carried out in rodents and consist of a single dose. In pharmaceutical drug development, this is the only study type where lethality or life-threatening toxicity is an endpoint as documented in current regulatory guidelines [22, 23.] To evaluate toxicity of a compound in animals various routes may be used, but two most commonly used modes of administration for animals studies are via intraperitoneal injection or the oral route [24].

Usually acute (single dose) toxicity study is carried out on laboratory animals by using high dose (sufficient to produce death or morbidity) of the substance in question and/or based on previous report on its toxicity or toxicity of structurally related compounds [25.] Acute toxicity studies are commonly used to determine LD_{50} of drug or chemicals [19]. The acute study provides a guideline for selecting doses for the sub-acute and chronic low dose study, which may be clinically more relevant [26, 27.]

Sub-acute toxicity:

In sub-acute toxicity studies, repeated doses of drug are given in sub-lethal quantity for a period of 14 to 21 days. Sub-acute toxicity studies are used to determine effect of drug on biochemical and hematological parameters of blood as well as to determine histopathological changes [19].

Chronic toxicity:

In chronic toxicity studies, drug is given in different doses for a period of 90 days to over a year to determine carcinogenic and mutagenic potential of drug [19]. The parameters of chronic toxicity studies are same as that of sub-acute study. Multiple dose studies are necessary to assure the safety of natural products.

On the other hand clinical observations of acute assays are valuable tools to define the doses to be tested in multiple dose experiments, along with pharmacological studies in animals and in humans [27, 28].

Importance of different parameters in toxicity study:

Gross behaviour assessment:

The gross behaviour assessment generally in mice can be evaluated by the model given by Morpugo [29]. The mice are placed one by one at the centre of three concentric circles drawn on a rubber sheet with diameter of 7cm, 14cm and 21cm. The animals are observed for different parameters of behavioural changes. After drug administration, the behaviour modifications were observed every hour till 5h and then at 24h, 48h and 72h. The mortality is observed for 10days after treatment. The observed results are recorded as the score of 0-3 point scale relative to the average intensity of the phenomena observed. Various parameters assessed for gross behaviour studies are CNS depression (Exitus, Hypoactivity, Passivity, Relaxation Narcosis, Ataxia, Ptosis); ANS effect (Exophthalmia, Hyperactivity, Irritability, Stereotypy) and CNS stimulation parameters (Tremors, Convulsions, Straub tail, Analgesia) and other Parameter- Mortality.

Body weight:

Body weight changes are indicators of adverse side effects, as the animals that survive cannot lose more than 10% of the initial body weight [30]. The determination of food and water consumption are important in the study of safety of a natural product, as proper intake of food and water are necessary to the physiological status of the animals and to the achievement of the proper response to the drug tested instead of a “false” response due to improper nutritional conditions [31].

Hematological importance:

The hematopoietic system is one of the most sensitive targets for toxic compounds and an important index of physiological and pathological status in man and animal [32]. The various hematological parameters investigated in this study are useful indices of evaluating the toxicity of plant extract in animals [33]. Assessment of hematological parameters are not only used to determine the extent of deleterious effect of extracts on the blood of animals, but it can also be used to explain blood relating functions of a plant extract or its products [34].

Hematological status is one of the important ways for the diagnosis of root cause of disease. Hematological disorders include a wide range of abnormal conditions indicating the profile of blood parameters, due to changes in metabolism. Alterations in blood parameters may be due to changes in cellular integrity, membrane permeability of cells or even due to exposure to toxic chemicals [35]. Reports regarding toxicological studies of plants on hematological aspects are scanty. However, some reports are available *viz.* [36, 37]. In hematological analysis the following parameters are measured: Red blood cells, Haemoglobin, Packed cell volume, Mean corpuscular volume, Mean corpuscular haemoglobin, Mean corpuscular haemoglobin concentration, Platelet Count, White blood cells, Neutrophils, Lymphocytes, Eosinophils, Monocytes and Basophils.

Each parameter has its own importance and increase or decrease in that particular parameter is indicative of specific disturbance. The fall in hemoglobin content, RBC count and PCV can be correlated with induction of anaemia, defective haematopoiesis, weakness and morbidity in experimental rats [38]. The increase in MCV and decrease in MCHC indicate macrocytic and hypochromic anemia [39]. WBC and its subpopulations relating to it such as lymphocytes usually show increase in activity in response to toxic environment [40].

The reduction in lymphocyte count and increase neutrophils count suggest some anti-lymphocytic activity [41]. Eosinophils normally constitute up to 7% of total circulating leukocytes. Eosinophils are important in the phagocytosis of foreign bodies. Eosinophils are also involved in allergic reactions [42]. Platelets also known as thrombocytes, help to mediate blood clotting, which is a meshwork of fibrin fibres. The fibres also adhere to damaged blood vessels; therefore, the blood clot becomes adherent to any vascular opening and thus prevents further blood clot [43].

Organ weight:

Organ weight changes have long been accepted as a sensitive indicator of chemically induced changes to organs and in toxicological experiments, comparison of organ weights between control and treated groups have conventionally been used to predict toxic effect of a test material [44, 45]. Organ weight is an index of swelling, atrophy or hypertrophy [46]. The relative organ weight is fundamental to diagnose whether the organ was exposed to the injury or not. The heart, liver, kidneys, spleen and lungs are the primary organs affected by metabolic reactions caused by toxicants. The liver is the major site of foreign compounds metabolism in the body [47].

In preclinical safety studies of new compounds, organ weight changes are often difficult to interpret in relation to primary compound effects when reductions in food consumption are also present. By gaining a better understanding of tissue changes caused solely by feed restriction, it may be possible to differentiate direct compound effects from those of inadequate nutrition. Various studies have yielded information about the effects of inadequate nutrition on body weights, organ weights, histologic tissue changes, and clinical pathology data in rats [48, 49].

On a body weight basis, it is assumed for toxicity data extrapolation that humans are usually about 10 times more sensitive than rodents. On a body surface–area basis, humans usually show about the same sensitivity as test mammals, i.e. the same dose per unit of body surface area will give the same given defined effect, in about the same percentage of the population. Knowing the above relationships, it is possible to estimate the exposure to a chemical that humans should be able to tolerate [50]. Body weight and internal organ such as liver, kidney, heart spleen, thymus glands, etc. are simple and sensitive indices of toxicity after exposure to toxic substance [30]**.** Toxicity data are required to predict the safety associated before the use of medical products [51].

Serum biochemical importance:

The serum biochemical tests are frequently used in diagnosis diseases of hearts, liver, kidney and cardiovascular system etc. They are also widely used in monitoring the response to exogenous toxic exposure [52]. When an herbal product is ingested, the body interacts with it in an attempt to get rid of any harmful toxins, especially if the body cannot

convert the foreign substance into cellular components. These insults are commonly manifested by changes in enzyme levels and other cell components. The enzymes commonly involved are glutamate oxaloacetate transaminase (AST/GOT) glutamate pyruvate transaminase (ALT/GPT), alkaline phosphatase (ALP). Also component like urea and uric acid are vital diagnostic tools for toxicity [53]. Generally, liver cell damage is characterized by a rise in serum enzymes like AST, ALT, ALP, etc. [54]. In general, GOT concentrations are consistently higher than ALT levels which are expected since body cells contain more AST than ALT. Usually, about 80% of AST is found in the mitochondria whereas ALT is purely cytosolic enzyme.

Therefore, AST appears in higher concentrations in a number of tissues (Liver, Kidney, heart and pancreas) and is released slowly in comparison to ALT. But since ALT is localized primarily in the cytosol of hepatocytes, this enzyme is considered a more sensitive marker of hepatocellular damage than AST and within limits can provide a quantitative assessment of the degree of damage sustained by the liver [55]. The urea and creatinine are good indicatiors for renal function. If kidney function falls, the urea and creatinine levels will rise [52].

Total protein measurement is used in the diagnosis and treatment of a variety of diseases involving the liver or kidney as well as other metabolic disorders. A decrease in albumin level has been attributed to several causes, such as massive necrosis of the liver, deterioration of liver function, hepatic resistance to insulin and glycogen impairment of oxidative phosphorylation [56]. Urea and creatinine are compounds derived from proteins which are eliminated by the kidney.

Table 1 lists some of the plants which show ethnomedicinal uses with botanical name, plant family, plant part (s) used and solvent used for extraction. Table 1 also provides information on toxicity study, route of administration and doses of plants. It lists toxicity studies *viz.* acute, sub-acute, chronic etc. with their doses, route of administration and LD_{50} values along with their safety profile. Determination of appropriate dose is a very important issue in the study of plant extracts. Therefore, before starting the study on plants, researchers should determine the dose of extract by referring the previous toxicity trials or do the toxicity workup by themselves.

In the above review, it is seen that in acute toxicity study, the dose is single but observations are carried out for 14 days, but it varied from 24 h to 19 days. In repeated dose studies, the dose is given daily or on alternate days. If done for 21-28 days it was called sub-acute toxicity study if continued for more days up to 90 days or more it was called chronic or sub-chronic toxicity study. The table also lists a number of plants and its toxicity profile so it becomes easy to carry out further work. It also helps in dose and route selection. The most common route was oral or i.p. Such review helps in knowing the toxicity level of different plants. If any pharmacological activity is done or to be done, this toxicity data will help to decide if that particular plant is safe or not.

TABLE 1: LIST OF MEDICINAL PLANTS, THEIR FAMILY, ETHNOMEDICINAL USES, PARTS AND SOLVENTS USED, TOXICITY STUDY, ROUTE OF ADMINISTRATION, DOSE LEVELS USED AND ITS SAFETY LEVEL

No.	Plants (family)	Ethnomedicinal uses	Parts used	Solvent	LD_{50} (g/kg) b.w. (route of administration)	Toxicity study (experimental periods), Dose (g/kg, b.w.) and route of administration	Result	Ref.
1.	*Acacia karroo* Hayne (Fabaceae)	Gum is an important food source	Stem, bark	Water	-	**Acute** (48 h) 0.4, 0.8, 1.6 and 3.2 (p.o.) **Sub acute** (14 days) 0.8 (p.o.)	Toxic	57
2.	*Acmela brasiliensis* DC	Respiratory infections and	Aerial parts	50% ET	-	**Acute** (24 h) 0.1, 0.5, 1, 2 and 4	Low toxicity	58

	(Asteraceae)	pain				(p.o.), **Sub acute** (15 days) 0.5, 1, 2 and 4 (p.o.)		
3.	*Aconium napeilus* Linn. (Ranunculaceae)	Pain, coldness, vertigo and general fatigue	Isolated alkaloid Aconitine	-	-	**Chronic** (22 days) 1 (p.o.)	Safe	59
4.	*Aframomum melegueta* (Roscoe) K. Schum. (Zingiberaceae)	Stomachache, diarrhea and snakebite	Seeds	95% ET	-	**Sub chronic** (28 days) 0.12, 0.45 and 1.5	Toxic (liver)	60
5.	*Ajuga iva* (L.) schreber (Labiatea)	Hyper tension, diabetes, gastrointestinal disorders and anthelmintic	Whole plant	Water	3.6 (i.p.)	**Acute** (14 days) 2, 4, 6, 10 and 14 (p.o.) 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5 and 5.5 (i.p.) **Chronic** (90 days) 0.1, 0.3, 0.6	Safe (p.o.) Toxic (i.p.)	61
6.	*Anacardium occidentale* L. (Anacardiaceae)	Gastrointestinal disorders, mouth ulcer, throat problems and hypertension	Leaves	70% ET	> 2	**Acute** (14 days) 2 (p.o) **Sub acute** (30 days) 0.40, 0.70, 1 (p.o)	Moderate toxicity	62
7.	*Anacardium occidentale* L. (Anacardiaceae)	Diabetes mellitus and inflammation	Leaves	HE	16 (p.o.)	**Acute** (7 days) 2, 6, 10, 14, 18, 22, and 26 (p.o.) **Chronic** (56 days) 6, 10 and 14	Toxic at high dose (chronic)	63
8.	*Anogeissus leiocarpus* (DC.) Guill. & Perr. (Combretaceae)	Helminthosis, schistosomiasis, leprosy, diarrhea and psoriasis	Leaves	Water	1.4 (i.p.)	**Acute** 72 h for p.o. and 24 h for i.p. 0.8, 1.2, 1.6, 2, 2.4, 2.8 (p.o. and i.p.)	Safe (oral) and low toxic (i.P.)	64
9.	*Artemisia afra* (Jacq. Ex. Willd) (Asteraceae)	Cough, colds, sore throat, heart burns, hemorrhoids, fever, malaria, asthma and diabetes mellitus	Leaves	Water	8.96 (p.o.) and 2.45 (i.p.)	**Acute** (14 days) 2, 4, 6, 8, 10, 12, 16, 20, and 24 (p.o.) 1.5, 2.5, 3.5, 4.5 and 5.5 (i.p.) **Chronic** (3 months) 0.01, 0.1, 1 (p.o.)	Safe	65
10.	*Asiasari radix* (Aristolochiaceae)	Neuroprotective	Whole plant	70% ME	-	**Acute** (14 days) 0.1, 0.3, 0.5 (p.o.)	Safe	66
11.	*Asparagus pubescens* Bak (Liliaceae)	Used as remedy for liver and kidney disorders	Roots	ME	-	**Acute** (24 h) 0.25 and 1 (p.o.)	Safe	67
12.	*Aspilia africana* (Pers) C.D. Adams (Compositae)	Stop bleeding, remove corneal opacities, anemia and various stomachs complains	Leaves	Water	6.6 (p.o.)	**Acute** (7 days) 2, 4, 8, 12 and 16 (p.o.) **Sub acute** (26 days) 0.5 and 1 (every 48 h) (p.o.)	Low toxicity	68
13.	*Basella alba* L. (Basellaceae)	Diarrhea, laxative and anemia	Leaves	Water	-	**Sub acute** 0.06, 0.08 and 0.1 (p.o.)	Safe	69
14.	*Bixa orellana* L. (Bixaceae)	Used in food industries	Isolated compound from annatto	-	-	**Sub acute** (28 days) 2 (p.o.)	Safe	70

15.	*Boerhavia diffusa* L.(Nyctaginaceae)	Inflammatory disorders, bacterial infection, heart diseases, corneal ulcers, antiviral and hepatic disorders	Leaves	Water	-	**Sub chronic** (30 days) 0.5, 1 and 2 (p.o.)	Safe	71
16.	*Boswellia dalzielii* Hutch.(Frankincense)	Wound healing, induce vomiting	Stem bark	Water	-	**Acute** (48 h) 3 (p.o.) **Sub chronic** (28 days) 0.9, 1.8 and 2.7 (p.o.)	Safe (acute) Toxic at high dose (sub chronic)	72
17.	*Bridelia ferruginea Benth* (Euphorbiaceae)	diabetes	Root bark	80% ET	-	**Acute** (14 days) 2 and 5 (p.o.) **Sub chronic** (28 days) 0.25, 0 .5 and 1.0 (p.o.)	Safe	73
18.	*Bryophyllum calycinum* Salisb. (Crassulaceae)	Antiviral, antimicrobial, antitumor, antioxidant, diuretic, antiulcer, anti-inflammatory, anti-diabetic	Leaves	ME and water	-	**Acute** (24 h) 0.5 to 3 (p.o.), 0.35 to 2.60 (i.p.)	Safe	74
19.	*Calendula officinalis* L. (Asteraceae)	Anti-inflammatory, wound healing and antiviral	Flowers	70% ET	-	**Acute** (14 days) 0.625, 1.25, 2.5 and 5 (p.o.) **Sub acute** (30 days) 0.025, 0.25, 0.5 and 1 (p.o.)	Safe	75
20.	*Calycopteris floribunda* Lam. (Combertaceae)	Dysentery, fever, emesis and ulcer	Leaves	ME, water	ME 0.38 (p.o)	**Acute** (14 days) 0.10, 0.20, 0.40, 0.60 (p.o)	ME - toxic water extract - safe	76
21.	*Camellia sinensis* (L.) Kuntze (Theaceae)	Antioxidant, anti-allergic, antiangiogenic, anti-inflammatory and hypolipidemic	Catechins	-	-	**Sub chronic** (90 days) 0.3, 1.25 and 5% (w/w) fed in diet	Safe up to 1.25 %	77
22.	*Careya arborea* Roxb. (Myrtaceae)	Anthelmintic, epileptic fits, bronchitis and astringents	Stem bark	ME	-	**Acute** (72 h) 0.1 to 1.6 (p.o.)	Safe	78
23.	*Carica papaya* L. (Caricaceae)	Anti-fertility	Seeds	ME	-	**Acute** (14 days) 2 (p.o) **Sub chronic** (28 and 90 days) 0.05, 0.1, 0.25 and 0.5 (p.o.)	Safe	79
24.	*Carrica papaya* L. (Caricaceae)	Digestive agent, wound healing, ulcer, boils and induce menstruation	Unripe fruit	Water	2.52 (p.o.)	**Acute** (24 h) 0.4, 0.8, 1.6 and 3.2 (p.o.) **Chronic** (42 days) 0.05, 0.1, 0.15, 0.2 and 0.25 (p.o.)	Safe	80

25.	*Cassia fistula* L. (Caesalpiniaceae)	Mild, pleasant purgative action, antifungal, antiviral, menstrual disorders and fever	Pods	Water	6.60 (i.p.)	**Acute** (48 h) 0.8, 1.6, 3.2, 6.4 and 12.8 (i.p.) **Sub chronic** (6 weeks) 0.25, 5 and 1 (i.p.)	Low toxic	81
26.	*Cassia sieberiana* DC (Caesalpiniaceae)	Urinogenital infection, antimicrobial and dysentery	Pod pulp	Water	1.95 (p.o.)	**Acute** (24 h) 1, 1.5, 2, 2.5 and 3 (p.o.) **Sub acute** (5 weeks) 0.2, 0.4, 0.8 and 1.6 (p.o.)	Toxic at high dose (sub acute)	82
27.	*Cassytha filiformis* R.Br. (Lauraceae)	Diabetes mellitus, ulcer and cough	Stems, leaves	Water	-	**Sub chronic** (28 days) 0.25, 0.5, 1 (p.o.)	Safe	83
28.	*Ceiba pentandra* L. (Bombacacease)	Antiameobic and antibacterial	Leaves	40% ME	-	**Acute** (24 h) 0.01 to 5 (p.o. **Chronic** (21 days) 0.25 to 5 (p.o.)	Safe	84
29.	*Centaurium erythraea*(L.) Rafn. (Gentianaceae)	sedative, antipyretic, asthma, jaundice, intestinal parasitic infestation, rheumatism, wounds and sores, blood pressure, edema and digestive disorders	Whole Plant	Water	0.12 (i.p.)	**Acute** (14 days) 1, 3, 5, 7, 9, 11, 13 and 15 (p.o.), 2, 4, 6, 8, 10, 12, 13 and 14 (i.p.) **sub-chronic** (90 days) 0.1, 0.6 and 1.2 (p.o.)	Safe	85
30.	*Chiococca alba* (L.) Hitchc (Rubiaceae)	Rheumatic disorders, emetic, antidiarrheic, purgative, diuretic, antipyretic, tonic and delayed menstruation	Roots	ET	-	**Acute** (14 days) 0.062, 0.125, 0.25, 0.5, 1 and 2 (p.o.), 0.062, 0.125, 0.25 and 0.5 (i.p. and s.c.) **Repeated** (14 days) 0.5, 1 and 2 (p.o.), 0.015, 0.013, 0.062 and 0.125 (i.p.)	Low toxicity (oral) Toxic (parenteral)	86
31.	*Cissampelos pareira* L. var hirsute (Menispermaceae)	Menstruation problems, pain reliever and used as remedy to control fertility temporarily	Roots	50% ET	-	**Acute** (13 days) 2 (p.o.) **Sub acute** (4 weeks) 1 and 2 (p.o.)	Safe	46
32.	*Crateva nurvala* Buch.-Ham. (Capparidaceae)	Digest, laxative, anthelmintic, antilithic, expectorant and antipyretic	Stem bark	PE, BZ,C, 95% ET, water	> 5 (p.o.)	**Acute** (14 days) 0.05 to 5 (p.o.)	Safe	87
33.	*Cucrbita maxima* Duch. (Cucurbitaceae)	Stomach pain, anti-inflammatory and antipyretic	Seeds	50% ET	> 5 (p.o.)	**Acute** (24h) 0.1, 0.5, 1 and 5 (p.o.), **Sub acute** (30 days) 1 (p.o.)	Safe	88
34.	*Cylicodiscus gabunensis* (Taub.) Harms (Mimosaceae)	Diarrhea and gastrointestinal disorders	Stem bark	EA	11 (p.o) for female and 14.5 (p.o.) for male	**Acute** (7 days)- 4, 8, 12 and 16 (p.o) **Sub acute** (6 weeks) 0.75, 1.5, 3 and 6 (p.o.)	Toxic at high dose	89

35.	*Datura stramonium* L.(Solanaceae)	Asthma, gastric pain, anti-inflammatory, stimulation of central nervous system and skin infection	Leaves	60% ET	-	**Chronic** (5 weeks) 0.05 and 0.2 (p.o.)	Safe	90
36.	*Delphinium denudatum* Wall (Ranunculaceae)	Anticonvulsion, anti-sterss, hepatoprotection, cardioprotection and antimicrobial	Roots	Water	16.1 (p.o.)	**Acute** (24 h) 14, 15, 16, 17, 18 and 24 (p.o)	Safe up to 16 g/kg b.w.	91
37.	*Dimorphandra mollis* Benth (Caesalpiniaceae)	Antioxidant, antiviral, anti-inflammatory, anti-tumor and anti platelets	Fruits	20% ET	-	**Acute** (13 days) 0.5, 2, 3.5 and 5 (p.o.)	Safe	17
38.	*Drimys angustifolia* Miers (Winteraceae)	Analgesic, antiulcer and anti-inflammatory	Leaves, stem bark	ET	-	**Acute** (48 h) 1.75, 3.5 and 5.25 (p.o.)	Toxic at high dose	92
39.	*Elephantorrhiza elephantina* (Burch.) Skeels. (Fabaceae)	diarrhoea, coughing, pneumoni and tick-borne diseases	Rhizomes	Water	-	**Acute** (24 h) 0.4, 0.8, 1.6 (p.o.) **Sub acute** (14 days) 0.2, 0.4, 0.8 (p.o.) **Chronic** (35 days) 0.05, 0.1, 0.2, 0.4 (p.o.)	Toxic at high dose	93
40.	*Entada africana* Guill. and Perr. (Mimosaceae)	Antileishmanial, anti-inflammatory, hepato-protective, respiratory tract disorders and wound healing	Stem bark, leaves	ME	Stem bark 0.146 and leaves 0.249 (i.p.)	**Acute** (72 h) 0.05 to 0.4 (i.p.)	Moderate toxic	94
41.	*Erythrina senegalensis* DC (Pailionaceae)	Bronchial infection, cough, and throat infection	Stem bark	C	0.526 (i.p.)	**Acute** (24 h) 0.1, 0.2, 0.4, 0.6 and 1.2 (i.p.) **Chronic** (12 weeks) 0.25, 0.5 and 1 (fed in diet)	Toxic at high dose	95
42.	*Euphorbia hirta* L (Euphorbiaceae)	Inflammation, respiratory tract and asthma	Leaves	ET, HE, EA, ME	-	**Repeated** (14 days) 0.4, 0.8 and 1.6 (p.o.)	Toxic	96
43.	*Ficus exasperata* (Vahl) (Moraceae)	Stimulant, ring worm and chest complications	Leaves, stem	98% ET		**Repeated** (3 days) 0.5, 0.1 and 0.5 (p.o)	Leaves were toxic while stems were safe	97
44.	*Ficus exasperata* (Vahl) (Moraceae)	Chest pain, eye troubles and stomach pains and to arrest bleeding	Leaves	Water	0.54 (i.p.)	**Acute** (24 h) 2.5, 5, 10 and 20 (p.o.) 0.1, 0.2, 0.4, 0.8 and 1 (i.p.)	Safe	98
45.	*Galega officinalis* L. (Papilionaceae)	Antidiabetic and increasing lactation	Aerial parts	Crude powder	-	**Acute** (14 days) 0.5, 1, 2.5 and 5 (p.o.) **Subchronic** (90 days) 0.15%, 1.5 %, and 3% (w/w) fed in diet	Safe (acute) Toxic (for liver and lung in Sub chronic)	99
46.	*Galphimia glauca* Cav. (Malpighiaceae)	Mental disorders, diminishing nervous excitement	Leaves	Water, ME, ET	-	**Sub chronic** (28 days) 2.5 (p.o.)	Safe	100

47.	*Garcinia haburyi* Hook. f. (Guttiferae)	Cytotoxic and anticancer activity	Gambogic acid (resin)	-	-	**Chronic** (13 weeks) 0.03, 0.06 and 0.12 (p.o.)	Safe	101
48.	*Glinuus lotoides* L. (Molluginaceae)	Anthelmintic	Seeds	60 % ME	-	**Acute** (14 days) 1 and 5 (p.o.) **Repeated** (28 days) 0.25, 0.5 and 1 (p.o.)	Safe	102
49.	*Gynura procumbens* (Merr.) (Compositae)	Eruptive fiver, rash, migraines, constipation, hypertension, diabetes mellitus, kidney diseases, and cancer	Leaves	ME	-	**Acute** (14 days) 1.25, 2.5 and 5 (p.o.) **Sub chronic** (90 days) 0.125, 0.25 and 0.5 (p.o.)	Safe	103
50.	*Helicteres isora* L. (Sterculiaceae)	Diabetes mellitus, colic, gastropathy, diarrhea and dysentery	Bark	Water	-	**Acute** (12 days) 2 (p.o.), **Repeated** (28 days) 0.5 (p.o.)	Safe	104
51.	*Ipomoea batatas* L. (Convolvulaceae)	Isolated compound ipomeamarone	Tuber	-	-	**Acute** (48 h) 0.25 and 0.5 (p.o.)	Toxic for liver	105
52.	*Jatropha curcus* L. (Euphorbiaceae)	Biodiesel	Phorbol (Isolated)	-	0.027 (p.o.)	**Acute** (19 days) 0.036, 0.032, 0.29, 0.026, 0.023 and 0.021 (p.o.)	Toxic	106
53.	*Kielmeyera coriaceae* Mart. (Clusiaceae)	Schistosomiasis, malaria, fungal and bacterial infections	Stem	DM	1.50 (p.o.) and 0.538 (i.p.)	**Acute** (14 days) 0.05, 0.2, 0.4, 0.8, 1.2, 1.8, 2 and 2.2 (p.o.) 0.05, 0.2, 0.4, 0.5, 0.6 and 0.8 (i.p.) **Repeated** (90 days) 0.005, 0.025 and 0.125 (p.o)	Safe	107
54.	*Kyllinga brevifolia* Rottb. Hassk (Cyperaceae)	Diuretic, sedative and antispasmodic properties	Rhizomes	70 % ET	0.575 (i.p.)	**Acute** 0.001, 0.01 and 0.1 (i.p.)	Safe	108
55.	*Laportea crenulata* Gaud (Urticaceae)	Weakness, asthma, gout, mumps, chronic fever	Roots	PE, C, ME	> 1 (i.p.)	**Acute** (24 h) 0.2 to 1 (i.p.)	Safe	109
56.	*Lonicera japonica* Thunb. (Caprifoliaceae)	Antipyretic, antibacterial, antiviral and antioxidant	Leaves	95% ET	-	**Acute** (14 days) 5 (p.o.) **Sub acute** (14 days) 1 (p.o.)	Safe	110
57.	*Macrothelypteris torresiana* (Gaud.) Ching Thelypteridacea)	Hydropsy and traumatic bleeding	Roots	EA	2.76 (p.o.), 0.87 (p.o.)	**Acute** (14 days) 6.67, 5, 3.75, 2.81, 2.11, 1.58, 1.19 and 0.89 (p.o.) 2.14, 1.57, 1.18, 0.89, 0.67, 0.50, 0.37 and 0.28 (p.o.) **Sub acute** (14 days) 6, 60, 600 and 1200 (p.o.), 4, 40, 400 and 800 (p.o.)	Low toxicity	111

58.	*Magnistipula butayei* Subsp. montana (Hauman) F. white (Chrysobalanceae	Trunk bark and root used as decoction and leaves and fruit used as killing wild animals (rats, dogs and other animals)	Trunk bark	Water	0.37 (p.o.)	**Acute** (3 days) 0.05, 0.1, 0.2, 0.4, 0.8 and 1.6 (p.o.)	Toxic	112
59.	*Mammea africanna* Sabine (Guttiferae)	Hypercholesterolemia, internal heat, microbial infection	Stem bark	Water	0.387 (i.p.)	**Acute** (24 h) 0.05 to 1 (i.p.) **Sub acute** (21 days) 0.03, 0.06 and 0.09 (p.o.)	Low toxic	113
60.	*Manihot esculenta* Crantz (Euphorbiaceae)	Human and animal nutrition and raw material for industrial products	Cassava	-	-	**Acute** (14 days) 5 ml/kg b.w. **Sub chronic** (28 days) 25%, 50%, and 100% ml/kg b.w.	Safe	114
61.	*Mitragyna inermis* (Willd.) O.Kuntze (Rubiaceae)	Malaria and fever	Leaves	60% ET	-	**Acute** (4 days) 0.30 and 3 (p.o.)**Chronic** (28 days) 0.30 to 3 (p.o.)	Toxic at high dose	115
62.	*Mitragyna speciosa* Korth (Rubiaceae)	analgesic, antipyretic, antidiarrheal and local anesthetic	Leaves	ME	-	**Acute** (14 days) 0.1, 0.5 and 1 (p.o.)	Severe hepatotoxic and mild nephrotoxic	116
63.	*Monascus purpureus* MTCC 410 (red mould rice)	Lowering blood pressure and blood cholesterol	-	-	-	**Acute** (14 days) 0.5, 1, 2.5 and 5 (fed in diet) **Sub chronic** (14 weeks) 2, 4, 8 and 12% w/w (fed in diet)	Safe	117
64.	*Murraya koenigii* (L.) spreng (Rutaceae)	Tonic, stomachic, anti-vomiting, dysentery, diarrhoea, hypoglycemic, febrifuge, antifungal and antiperiodic	Leaves	ME	0.316 (p.o.)	**Acute** (72 h) 0.2, 0.5, 1 and 2 (p.o.) **Sub chronic** (14 days) 0.25, 0.35 and 0.45 (p.o.)	Toxic at high dose	118
65.	*Musanga cecropioides* R.Br. (Cecreopiaceae)	Rheumatism, leprosy and chest infection	Stem bark	Water	-	**Acute** (12 days) 3 (p.o.) **Repeated** (28 days) 0.75 (p.o.)	Safe	119
66.	*Ocimum suave* wild. (Lamiaceae)	Ulcers, anticathartic, mosquito repellent and analgesic	Leaves	Water	-	**Acute** (7 days) 2 and 8 (p.o.) **Sub acute** (6 weeks) 0.25, 0.5 and 1 (p.o.)	Safe	120
67.	*Pluchea arguta* Boiss (Compositeae)	Antiinflammatory, antioxiant	Leaves	ME	- (p.o.)	**Acute** (7 days) 1,3 and 6 (p.o.)	Safe	121
68.	*Polygala fruticos* (P.J. Bergius) (Polygalaceae)	Chronic ulcer, poor circulation, intestinal sores, gonorrhoea and the snuff to improve sinusitis	Leaves	Water	10.8 (p.o.)	**Acute** (14 days) 2, 4, 8, 12, 16 and 20 (p.o.) **Sub chronic** (31 days) 0.1 to 1 (p.o.)	Toxic at high dose	122

69.	*Polyalthia longifolia* (Sonn.) Thw(Annonacea)	Treatment of fever, skin disease, diabetes, hypertension	Leaves	ME	- (p.o.)	**Acute** (7 days) .54,1.1,2.1 and 3.2 (p.o.)	Safe	123
	Pongamia pinnata (L.) Merr. (Papilionaceae)	Anticonvulsant, hypotensive effects, bronchitis, chronic fever, whooping cough, and skin diseases	Pongamol (isolated)	-	-	**Sub acute** (14 days) 300 µg/0.3 ml (i.p.)	Safe	19
70.	*Portulaca grandiflora* Hook. (Portulaceae)	Sore throat, skin rash and detoxification	Aerial part	Water	-	**Chronic** (6 months) 0.01, 0.1 and 1(p.o.)	Safe	124
71.	*Pothomorphe umbellate* L. Miq. (Piperaceae)	Liver and inflammation disorders	Roots	50% ET	-	**Acute** (14 days) 1, 2, and 5 (p.o) **Sub chronic** (40 days) 0.5 (p.o.)	Safe	125
72.	*Salacia oblonga* Wall. (Celastaceae)	Used as remedy for diabetes	Whole plant	Water	-	**Sub chronic** (90 days) 0.25, 1.25 and 2.5 (p.o)	Safe up to 0.25 g/kg	126
73.	*Salvia przewalskii* Maxim (Labiatae)	coronary heart diseases, myocardial infarction and atherosclerosis, angina pectoris and liver diseases	Rhizomes	ET	2.54 (p.o.), 0.90 (i.m.), 0.78 (i.p.)	**Acute** (14 days) 1.72, 1.98, 2.27, 2.62, 3.01 and 3.46 (p.o.), 0.288, 0.412, 0.58, 0.84, 1.2 and 1.71 (i.m.) 0.5, 0.625, 0.781, 0.977, 1.22 and 1.52 (i.p.) **Sub acute** (30 days) 0.05 and 0.25 (p.o.)	Safe	127
74.	*Salvia scutellarioides* Kunth (Lamiaceae)	Antihypertensive and diuretic properties	Bark, leaves	Water	-	**Acute** (14 days) 2 (p.o.) **Sub acute** (4 weeks) 1 and 2 (p.o.)	Safe	128
75.	*Schinus molles* var areira (Anacardiaceae)	Antibacterial, antiviral, antiseptic, astringent, digestive, purgative, diuretic, tooth ache, wound healer, menstrual disorders and rheumatism	Fruits	ET	-	**Acute** (14 days) 2 (p.o) **Sub-acute** (14 days) 1 (p.o)	Safe	129
76.	*Schinus terebinthifolius* Raddi (Anacardiaceae)	ulcers, gout, tumors, respiratory problems, wounds, rheumatism, diarrhea, skin ailments, arthritis, antiseptic, anti-inflammatory, balsamic and haemostatic	Stem bark	70% ET	-	**Acute** (14 days) 0.625, 1.25, 2.5 and 5 (p.o.) **Sub acute** (45 days) 0.25, 0.625 and 1.5625	Safe	130

77.	*Semecarpus anacrdium* L. (Anacardiaceae)	Asthma, piles digestive disorders, cardiac tonic, antimicrobial, anticancer and anti-inflammatory	Fruits (oil)	-	-	**Sub acute** (7 days) 0.25, 0.5 and 0.75 (p.o.) (21 days) 0.083 and 0.166 (p.o.)	Toxic	131
78.	*Senna alata* (L.) Roxb. (Ceasalpiniaceae)	Hepatitis and skin diseases	Leaves	Water and ET	18.5 (p.o.)	**Acute** (8 days) 4, 8, 12, 16 and 20 (p.o.) **Sub acute** (28 days) 0.5 and 1 (every 48 h) (p.o.)	Safe	132
79.	*Sida cordifolia* L. (Malvaceae)	Stomatitis of asthma and nasal congestion	Leaves	70% ET	2.64 (i.p.)	**Acute** (48 h) 0.5 to 5 (p.o.), 0.5 to 3 (i.p.)	Safe (p.o.) Toxic at high dose (i.p.)	133
80.	*Sida rhombifolia* L. (Malvaceae)	Antiseptic, wound-healing activity, diarrhea, cough, ulcer	Whole plant	Water / ME	-	**Acute** (24 h) 4, 8, 12 and 16 (p.o.)	Toxic at high dose	134
81.	*Smilax kraussiana* (Liliaceae)	Inflammation	Leaves	ME	0.24 (i.p.)	**Acute** (24 h) 0.01 to 1 (i.p.)	Safe up to 0.24 g/kg b.w. (i.p.)	135
82.	*Sphenocentrum Jollyanum* Pierre (Menispermaceae)	Vermifuge, chronic wound, cough and anti-inflammatory	Leaves	ET	1.44 (i.p.)	**Acute** (24 h) 11 (p.o.) 0.25 to 4 (i.p.) **Sub chronic** (120 days) 0.05, 0.1 and 0.2 (p.o.)	Safe	37
83.	*Stachtarpheta cayennensis* (Verbanaceae)	Stomachic, febrifuge and chronic liver diseases	Leaves	Water, 50 % ET, BT, EA	50% ET extract 0.09 (i.p.) in mice	**Acute** (72 h) **Rat-** 0.25, 0.5 and 1 (i.p.) **Mice-** 0.005 to 0.1 (i.p.) and 0.05 to 0.25 (p.o.)	50% ET extract was toxic in mice other extract were safe	136
84.	*Striga hermonthica* (Del.) Benth (Scrophulariacea)	Dermatosis, leprosy, jaundice and antibacterial	Leaves, flowers, stem	80% A	17.53 (i.p.)	**Acute** (24h) 15.5, 16.5, 17.5, 18.5, 21.5 and 23 (i.p.)	Safe up to 17.53 g/kg b.w.	137
85.	*Strychnos potatorum* L (Loganiaceae)	Astringent, refrigerant, emetic, antithelmintic, diuretic, digestive, tonic, stomachic, ophthalmic, appetizer, water purifier and relive colic	Seed	Water	-	**Acute** (72 h) 0.05, 0.3 and 2 (p.o.) **Chronic** (90 days) 0.1 and 0.2 (p.o.)	Safe	138
86.	*Stryphnodendron adstringens* (Martius) coville (Leguminosae)	Anti-inflammatory, analgesic and gastric mucosa	Stem, bark	Water	-	**Acute** (7 days) 2 (p.o.) **Sub acute** (30 days) 0.80 and 1.60 (p.o.)	Safe (acute) Toxic (sub acute)	139
87.	*Syzygium cumini* L. (Myrtaceae)	Diabetes, high blood pressure, diarrhea and fever	Stem, bark, leaves	70% ME	Leaves 0.387 (p.o.) Stem bark > 5 (p.o.)	**Acute** (24 h) 0.01, 0.1 and 1 (p.o.)	Safe	140
88.	*Syzygium cumini* L.(Myrtaceae)	Hypoglycemic, anti-HIV, antibacterial and anti-diarrheal	Seeds	EA, ME		**Acute** (14 days) 0.05, 0.3 and 2 (p.o)	Safe	141

89.	*Tamarindus indica* L. (Fabaceae)	Cold, jaundice, stomach disorders, diarrhea, fever and skin cleanser	Pulp	Water	-	**Sub acute** (28 days) 0.9, 1.8, 2.7, 3.6 and 4.5 (p.o.)	Safe	142
90.	*Tanacetum vulgare* L. (Asteraceae/compositae)	Menstrual irregularities, anthelmic, carminative, antispasmodic, stimulant and tonic properties	Leaves	Water	9.9 (p.o.) and 2.8 (i.p.)	**Acute** (14 days) 1 to 13 (p.o.) 1, 1.5, 2, 2.5, 3, 3.5, 4 and 4.5 (i.p.) **Chronic** (90 days) 0.1, 0.2 and 0.6 (p.o.)	Safe	143
91.	*Tetrapleura tetraptera* (Schumach. & Thonn.) Taub. (Mimosaceae)	Convulsion, leprosy, inflammation, jaundice, rheumatism, flatulence	Fruit	80% ET	-	**Sub acute** (10 days) 0.05, 0.1 and 0.15 (p.o.)	Toxic	144
92.	*Tithonia diversifolia* (Hemsl) (Asteraceae)	Malaria, menstrual pains, diabetes mellitus, sore throat, liver and measles	Leaves	Water	-	**Repeated** (7 days) 0.1 and 0.2 (p.o.)	Toxic (liver, heart and kidney)	145
93.	*Tithonia diversifolia* (Hemsl.) (Asteraceae)	Malaria, diarrhea, bacterial and parasitic infection	Leaves	Water	0.12 (p.o)	**Acute** (24 h) 0.05, 0.08, 0.1, 0.12 and 0.14 (p.o.)	Toxic	146
94.	*Toona sinensis* Roemor (Meliaceae)	Carminative enteritis and dysentery	Leaves	Water	-	**Acute** (14 days) 5 (p.o.) **Sub acute** (28 days) 1 (p.o.)	Safe	147
95.	*Vernonia amygdalina* Del (Compositae)	Antimalaria, anticancer, antimicrobial, as laxative herbs and anthelmintics	Leaves	95% ME, HE, EA, ME	-	**Sub acute** (6-fraction) (28 days) 0.08, 0.16 and 0.32 (p.o.)	Safe	148
96.	*Vernonia condensate* Baker (Asteraceae)	Gastro intestinal disorders, headache, diarrhea and protection against snakebites	Leaves	Water	-	**Acute** (0.30, 0.45, 0.67, 1, 1.5, 2.25, 3.4 and 5 (p.o. and i.p.)	Safe	149
97.	*Zingiber zerumbet* Smith. (Zingiberaceae)	Anticancer and cytotoxic activity	Zerumbone from rhizomes	-	1.84 (i.p.)	**Acute** (48 h) 0.1, 0.2, 0.5, 1, 1.5, 2, 2.5 and 3 (i.p.)	Toxic at high dose	150

A – acetone, BT – butanol, BZ – benzene, C – chloroform, DM – dichloromethane, EA – ethyl acetate, ET – ethanol, HE – hexane, ME – methanol, PE – petroleum ether, p.o. – per oral, i.p. –intraperitoneally, s.c. – subcutaneous, i.m. – intramuscular

ACKNOWLEDGEMENTS: The authors thank Prof. S.P. Singh, Head, Department of Biosciences, Saurashtra University, Rajkot, Gujarat, India for providing excellent research facilities.

REFERENCES:

1. Cragg MG, Newman DJ. Natural product drug discovery in the next millennium. Pharmaceutical Biology 2001; 39:8-17.
2. Farnsworth NR. The role of medicinal plants in drug development. In: Krogsgaard-Larson P, Brogger CS and Munksgaard H, editors. Natural Products and Drug Development, Alfred Benzon Symposium, Copenhagen, Denmark, Munksgaard, pp.17-30, 1984.
3. Zhu M, Lew KT, Leung P. Protective effect of plant formula on ethanol induced gastric lesions in rats. Phytotherapy Research 2002; 16: 276-280.
4. Sofowora EA. Medicinal Plants and Traditional Medicine in Africa 1st edition, Spectrum Books Ltd. Ibadan, Nigeria, 1989.
5. Whitto PA, Lau A, Salisbury A, Whitehouse J, Evans CS. Kava lactones and the kava-kava controversy. Phytochemistry 2003; 64:673-679.
6. Izzo A. Drug interactions with St. John's Wort (Hypericum perforatum): A review of the clinical evidence. International Journal of Clinical Pharmacology and Therapeutics 2004; 42:139-148.

7. Seth SD, Sharma B. Medicinal plants in India. Indian Journal Medical Research 2004; 120:9-11.
8. Gesler WM. Therapeutic landscapes: medicinal issues in light of the new cultural geography. Social Science and Medicine 1992; 34:735-746.
9. Bent S, Ko R. Commonly used herbal medicines in the United States: A review. The American Journal of Medicine 2004; 116: 478-485.
10. Duffus JH, Worth HGJ. Introduction to Toxicology. In: Fundamental Toxicology 2nd edition, RSC publishing, UK, 2006.
11. Talalay P, Talalay P. The importance of using scientific principles in the development of medicinal agents from plants. Academic Medicine 2001; 76: 238-247.
12. Timbrell JA (2002). Introduction to Toxicology 3rd edition, Taylor and Francis, USA, pp. 1-15, 2002.
13. Ozbek H, Ozturk M, Ozturk A, Ceylan E, Yener Z. Determination of lethal doses of volatile and fixed oils of several plants. Eastern Journal of Medicine 2004; 9:4-6.
14. Da Silva J, Herrmann SM, Heuser V, Peres W, Marroni NP, Gonzalez-Gallego J, Erdtmann B. Evaluation of the genotoxicity affect of rutin and quercetina by comet assay and micronucleus test. Food and Chemical Toxicology 2002; 40: 941-947.
15. Alvarez L, Gil AG, Ezpeleta O, Jalon-Garcıa JA, Cerain L. Immunotoxic effects of Ochratoxin A in Wistar rats after oral administration. Food and Chemical Toxicology 2004; 42: 825-834.
16. Eaton DL, Klaassen CD. Principle of Toxicology. In: Casarett and Doull's Toxicology. The Basic Sciences of Poisons 5th edition, (Ed Klaassen CD) McGraw-Hill, New York, pp.13-33, 1996.
17. Feres CAO, Madalosso RC, Rocha OA, Leite JPV, Guimaraes TMDP, Toledo VPP, Tagliati CA. Acute and chronic toxicological studies of *Dimorphandra mollis* in experimental animals. Journal of Ethnopharmacology 2006; 108: 450-456.
18. Anisuzzaman ASM, Sugimoto N, Sadik G, Gufor MA. Sub-acute toxicity study of 5-hydroxy-2 (hydroxyl-methyl) 4H-pyran-4-one, isolated from *Aspergillus fumigates*. Pakistan Journal of Biological Science 2001; 4:1012-1015.
19. Baki MA, Khan A, Al-Bari MAA, Mosaddik A, Sadik G, Mondal K. Sub-acute toxicological studies of Pongamol isolated from *Pongamia pinnata*. Research Journal of Medicine and Medical Sciences 2007; 2:53-57.
20. Hayes AW. Principles and Methods of Toxicology 4th edition, Raven Press, New York, 2001.
21. University of Wisconsin Chemical Safety and Disposal Guide (UWCSDG). Chemical and Environmental Safety Program, University of Wisconsin-Madison 30 N. Murray St., Madison, WI. 53715-2609, 1999.
22. Center for Drug Evaluation and Research (CDER). Guidance for Industry. Single Dose Acute Toxicity Testing for Pharmaceuticals. Food and Drug Administration (FDA), USA, pp.1-2, 1996.
23. Commission Directive. Amending Directive 2001/83/EC of the European Parliament and of the Council on the Community Code Relating to Medicinal Products for Human Use (63/EC of the 25th June 2003). Annex I, Official Journal of the European Communities L159 27/6/ 2003, Brussels, pp. 46-94, 2003.
24. Poole A, Leslie GB. A Practical Approach to Toxicological Investigations 1st edition, Great Britain, Cambridge University Press Vol. 2, 1989.
25. Demma J, Gebre-Mariam T, Asres K. Toxicological study on *Glinus lotoides*: A traditionally used taenicidal herb in Ethiopia. Journal of Ethnopharmacology 2007; 111:451-457.
26. Janbaz KH, Saeed SA, Gilani AU. Protective effect of rutin on paracetamol- and CCl_4-induced hepatotoxicity in rodents. Fitoterapia 2002; 73:557-563.
27. Hasumura M, Yasuara K, Tamura T, Imai T, Mitsumori K, Hirose M. Evaluation of the toxicity of enzymatically decomposed rutin with 13-weeks dietary administration to Wistar rats. Food and Chemical Toxicology 2004; 42: 439-444.
28. Alvarez L, Gil AG, Ezpeleta O, Jalon-Garcıa JA, Cerain L (2004). Immunotoxic effects of Ochratoxin A in Wistar rats after oral administration. Food and Chemical Toxicology 42, 825-834.
29. Morpugo C. A new design for the screening of CNS-active drugs in mice. Arzneimittel Forschung 1971; 11:1727-1734.
30. Teo S, Stirling D, Thomas S, Hoberman A, Kiorpes A, Khetani V. A 90-day oral gavage toxicity study of D-methylphenidate and D, L-methylphenidate in Sprague Dawley rats. Toxicology 2002; 179:183-196.
31. Stevens KR, Mylecraine L. Issues in Chronic Toxicology. In: Principles and Methods of Toxicology 3rd edition, (Ed Hayes AW) Raven Press, New York, pp. 673, 1994.
32. Mukinda JT, Syce JA. Acute and chronic toxicity of the aqueous extract of *Artemisia afra* in rodents. Journal of Ethnopharmacology 2007; 112:138-144.
33. Toyin YM, Adewumi AM, Temidayo OA. Alterations in serum lipid profile of male rats by oral administration of aqueous extract of *Fadogia argrestis* stem. Research Journal of Medicinal Plants 2008; 2: 66-73.
34. Toyin YM, Adewumi AM, Temidayo OA. Hematological evaluation in male albino rats following chronic administration of aqueous extract of *Fadogia agrestis* stem. Pharmacognosy Magazine 2007; 3: 34-38.
35. Hoffbrand AV, Pettit JE. Essential of Heamatology 3rd edition, Blackwell Sci Inc., USA, 1997.
36. Bafor EE, Igbinuwen O. Acute toxicity studies of the leaf extract of *Ficus exasperata* on haematological parameters, body weight and body temperature. Journal of Ethnopharmacology 2009; 123:302-307.
37. Mbaka GO, Adeyemi OO, Oremosu AA. Acute and sub-chronic toxicity studies of the ethanol extract of the leaves of *Sphenocentrum jollyanum* (Menispermaceae). Agriculture and Biology Journal of North America 2010; 1:265-272.
38. Criswell K, Sulhanen A, Hochbaum AF, Bleavens M. Effect of PHZ or phlebotomy on peripheral blood, bone marrow and erythropoietin Wistar rats. Journal of Applied Toxicology 2002; 20:25-29.
39. Barger AM. The complete blood cell count: a powerful diagnostic tool. Veterinary Clinics of North America - Small Animals 2003; 33: 1207-1222.
40. Robins SL. Lymph Nodes and Spleen. In: Pathologic Basis of Disease, Saunders WB, editor, Philadelphia, 1974.
41. Garg SK, Shah MAA, Garg KM, Farooqui MM, Sabir M. Anti lymphocytic and immunosuppressive effects of *Lantana camara* leaves in rats. Indian Journal of Experimental Biology 1997; 35:1315-1318.
42. Oyesanmi O, Kunkel EJS, Daniel AM, Howard lF. Hematologic side effects of psychotropics. Psychosomatics 1999; 40:414–421.
43. Andrews RK, Lopez JA, Berndt MC. Molecular mechanisms of platelet adhesion and activation. The International Journal of Biochemistry & Cell Biology 1997; 29:91-105.

44. Pfeiffer CJ. A mathematical evaluation of the thymic weight parameter. Toxicology and Applied Pharmacology 1968; 13:220-227
45. Nisha A, Muthukumar SP, Venkateswaran G. Safety evaluation of arachidonic acid rich *Mortierella alpina* biomass in albino rats-a subchronic study. Regulatory Toxicology and Pharmacology 2009; 53: 186-194.
46. Amresh G, Singh PN, Rao CV (2008). Toxicological screening of traditional medicine Laghupatha (*Cissampelos pareira*) in experimental animals. Journal of Ethnopharmacology 2008 ; 116:454-460.
47. Dybing E, Doe J, Groten J, Kleiner J, O'Brien J, Renwick AG, Schlatter J, Steinberg P, Tritscher A, Walker R, Younes M. Hazard characterisation of chemicals in food and diet: dose response, mechanisms and extrapolation issues. Food and Chemical Toxicology 2002; 40: 237–282.
48. Oishi S, Oishi H, Hiraga K. The effect of food restriction for 4 weeks on common toxicity parameters in male rats. Toxicology and Applied Pharmacology 1979; 47:15-22.
49. Levin S, Semler D, Ruben A. Effects of two weeks of feed restriction on some common toxicologic parameters in Sprague-Dawley rats. Toxicology and Pathology 1993; 21:1-14.
50. Duffus JH, Worth HGJ. Introduction to Toxicology. In: Fundamental Toxicology 2nd edition, RSC publishing, UK, 2006.
51. McNamara B. Concepts in Health Evaluation of Commercial and Industrial Chemical. In: Mehlman MA, Shapiro RE, Blumental H editors, New Concepts in Safety Evaluation, Hemisphere, Washington DC, Vol. 1, 1976.
52. Wang B, Feng WF, Wang TC, Jia G, Wang M, Shi JW, Zhang F, Zhao YL, Chai ZF. Acute toxicity of nano- and micro-scale zinc powder in healthy adult mice. Journal of Ethnopharmacology 2006; 161:115-123.
53. Dapar LP, Aguiyi CJ, Wannang NN, Gyang SS, Tanko MN. The histopathologic effects of *Securidaca longepedunculata* on heart, liver, kidney and lungs of rats. African Journal of Biotechnology 2007; 6:591-595.
54. Brautbar N, Williams IIJ. Industrial solvents and liver toxicity: risk assessment, risk factors and mechanisms. International Journal of Hygiene and Environmental Health 2002; 205:479-491.
55. Al Mammary M, Al-Habori M, Al-Aghbari AM, Baker MM. Investigation into the toxicological effects of *Catha edulis* leaves: a short-term study in animals. Phytotherapy Research 2002; 16:127-132.
56. Rao RH. Fasting glucose homeostasis in the adaptation to chronic nutritional deprivation in rats. American Journal of Physiology 1995; 268:873–879.
57. Adedapo AA, Sofidiya MO, Masika PJ, Afolayan AJ. Safety evaluation of the aqueous extract of *Acacia karroo* stem bark in rats and mice. Records of Natural Products 2008; 2: 128-134.
58. Burger C, Fischer DR, Cordenunzzi DA, Batschauer APB, Filho VC, Soares ARS. Acute and subacute toxicity of the hydroalcoholic extract from Wedelia paludosa (*Acmela brasiliensis*) (Asteraceae) in mice. Journal of Pharmacy and Pharmaceutical Sciences 2005; 8:370-373.
59. Wada K, Nihira M, Ohno Y. Effects of chronic administration of aconitine on body weight and rectal temperature in mice. Journal of Ethnopharmacology 105:89-94.
60. Ilic N, Schmidta BM, Pouleva A, Raskina I. Toxicological evaluation of grains of Paradise (*Aframomum melegueta*) [Roscoe] K. Schum. Journal of Ethnopharmacology 2010; 127: 352-356.
61. Hilaly JE, Israili ZH, Lyoussi B. Acute and chronic toxicological studies of *Ajuga iva* in experimental animals. Journal of Ethnopharmacology 2004; 91:43-50.
62. Konan NA, Bacchi EM, Lincopan N, Varela SD, Varanda EA. Acute, subacute toxicity and genotoxicity effect of a hydroethanolic extract of the cashew (*Anacardium occidentale* L.). Journal of Ethnopharmacology 2007; 110:30-38.
63. Tedong L, Dzeufiet PDD, Dimo T, Asongalem EA, Sokeng SN, Flejou JF, Callard P, Kamtchouing P. Acute and subchronic toxicity of *Anacardium occidentale* Linn. (Anacardiaceae) leaves hexane extract in mice. African Journal of Traditional, Complementay and Alternaive Medicines 2007; 4:140-147.
64. Agaie BM, Onyeyili PA, Muhammad BY, Ladan MJ. Acute toxicity effects of the aqueous leaf extract of *Anogeissus leiocarpus* in rats. African Journal of Biotechnology 2007; 6:886-889.
65. Mukinda JT, Syce JA. Acute and chronic toxicity of the aqueous extract of *Artemisia afra* in rodents. Journal of Ethnopharmacology 2007; 112:138–144.
66. Ramesh T, Lee K, Lee HW, Kim SJ. Acute oral toxicity study of *Asiasari radix* extract in mice. International Journal of Toxicology 2007; 26:247-251.
67. Nwafor PA, Jacks TW, Longe OO. Acute toxicity study of methanolic extract of *Asparagus pubescens* root in rats. African Journal of Biomedical Research 2004; 7:19-21.
68. Taziebou Lienon C, Etoa FX, Nkegoum B, Pieme CA, Dzeufiet DPD. Acute and subacute toxicity of *Aspilia africana* leaves. African Journal of Traditional, Complementay and Alternaive Medicines 2007; 4:127-134.
69. Bamidele O, Akinnuga AM, Olorunfemi JO, Odetola OA, Oparaji CK, Ezeigbo N. Effects of aqueous extract of *Basella alba* leaves on haematological and biochemical parameters in albino rats. African Journal of Biotechnology 2010; 9:6952-6955.
70. Bautista ARPL, Moreira ELT, Batista MS, Miranda MS, Gomes ICS. Subacute toxicity assessment of annatto in rat. Food and Chemical Toxicology 2004; 42:625-629.
71. Orisakwe OE, Afonne OJ, Chude MA, Obi E, Dioka CE. Sub-chronic toxicity studies of the aqueous extract of *Boerhavia diffusa* leaves. Journal of Health Science 2003; 49:444-447.
72. Etuk EU, Agaie BM, Onyeyili PA, Ottah CU. Toxicological studies of aqueous stem bark extract of *Boswellia dalzielii* in albino rats. Indian Journal of Pharmacology 2006; 38:359-360.
73. Bakoma B, Berké B, Gadegbeku KE , Agbonon A, Aklikokou K, Gbeassor M, Creppy EE, Moore N. Acute and sub-chronic (28 days) oral toxicity evaluation of hydroethanolic extract of *Bridelia ferruginea* Benth root bark in male rodent animals. Food and Chemical Toxicology 2013; 52:176-179.
74. Devbhuti D, Gupta JK, Devbhuti P, Bose A. Phytochemical and acute toxicity study on *Bryophyllum calycinum* salisb. Acta Poloniae Pharmaceutica Drug Research 2008; 65:501-504.
75. Silva EJR, Goncalves ES, Aguiar F, Evencio LB, Lyra MMA, Coelho MCOC, Fraga MCCA, Almir G. Toxicological studies on hydroalcoholic extract of *Calendula officinalis* L. Phytotherapy Researcch 2007; 21:332-336.
76. Sreekanth P, Narayana K, Shridhar NB, Avinash B. Toxicity studies of *Calycopteris floribunda* Lam. in calf, rabbit and rat. Journal of Ethnopharmacology 2006; 107:229-233.

77. Takami S, Imai T, Hasumura M, Cho YM, Onose J, Hirose M. Evaluation of toxicity of green tea catechins with 90-day dietary administration to F344 rats. Food and Chemical Toxicology 2008; 46:2224-2229.
78. Samdath Kumar R, Sundram RS, Sivakumar P, Nethaji R, Senthil V, Murthy NV, Kanagasabi R. CNS activity of the methanol extracts of *Careya arborea* in experimental animal model. Bangladesh Journal of Pharmacology 2008; 3:36-43.
79. Lohiya NK, Manivannan B, Garg S. Toxicological investigations on the methanol sub-fraction of the seeds of *Carica papaya* as a male contraceptive in albino rats. Reproductive Toxicology 2006; 22:461-468.
80. Oduola T, Adeniyi FAAA, Ogunyemi EO, Bello IS, Idowu TO, Subair HG. Toxicity studies on an unripe *Carica papaya* aqueous extract: biochemical and haematological effects in Wistar albino rats. Journal of Medicinal Plants Research 1:1-4.
81. Akanmu MA, Iwalewa EO, Elujoba AA, Adelusola KA. Toxicity potentials of *Cassia fistula* fruits as laxative with reference to senna. African Journal of Biomedical Research 2007; 7:23-26.
82. Toma I, Karumi Y, Geidam MA. Phytochemical screening and toxicity studies of the aqueous extract of pods pulp of *Cassia sieberiana* DC. (*Cassia kotchiyana* Oliv.). African Journal of Pure and Applied Chemistry 2009; 3:26-30.
83. Babayi HM, Udeme JJI, Abalaka JA, Okogun JI, Salawu OA, Akumka DD, Adamu HND, Zarma SS, Adzu BB, Abdulmumuni SS, Ibrahime K, Elisha BB, Zakariya SS, Inyang US. Effect of oral administration of aqueous whole extract of *Cassytha filiformis* on haematograms and plasma biochemical parameters in rats. Journal of Medical Toxicology 2007; 3:146-151.
84. Sarkiyayi S, Ibrahim S, Abubakar MS. Toxicological studies of *Ceiba pentandra* Linn. African Journal of Biotechnology 2009; 3:279-281.
85. Tahraoui A, Israili ZH, Lyoussi B. Acute and sub-chronic toxicity of a lyophilised aqueous extract of *Centaurium erythraea* in rodents. Journal of Ethnopharmacology 2010; 132:48–55.
86. Gazda VE, Carneiro MRG, Barbi NS, Paumgartten FJR. Toxicological evaluation of an ethanolic extract from *Chiococca alba* roots. Journal of Ethnopharmacology 2006; 105:187-195.
87. Sikarwar MS, Patil MB, Kokate CK, Sharma S, Bhat V. Pharmacognostical, phytochemical screening and acute toxicity study of *Crateva nurvala* stem bark. Pharmacognosy Journal 2009; 1:116-120.
88. Cruz RCB, Meurer CD, Silva EJ, Schaefer C, Santos ARS, Cruz AB, Filho C. Toxicity evaluation of *Cucurbita maxima* seed extract in mice. Pharmaceutical Biology 2006; 44: 301-303.
89. Kouitcheu MLB, Beng V, Kouam J, Essame O, Etoa FX. Toxicological evaluation of ethyl acetate extract of *Cylicodiscus gabunensis* stem barks (Mimosaceae). Journal of Ethnopharmacology 2007; 111:598-606.
90. Gidado A, Zainab AA, Hadiza MU, Serah DP, Anas HY, Milala MA. Toxicity studies of ethanol extract of the leaves of *Datura stramonium* in rats. African Journal of Biotechnology 2007; 6:1012-1015.
91. Zafar S, Ahmad MA, Siddiqui TA. Acute toxicity and antinociceptive properties of *Delphinium denudatum*. Pharmaceutical Biology 2003; 41:542-545.
92. Witaicenis A, Roldao EF, Seito LN, Rocha NP, Stasi LCD. Pharmacological and toxicological studies of *Drimys angustifolia* Miers. (Winteraceae). Journal of Ethnopharmacology 2007; 111:541-546.
93. Maphosa V, Masika PJ, Moyo B. Toxicity evaluation of the aqueous extract of the rhizome of *Elephantorrhiza elephantina* (Burch.) Skeels. (Fabaceae), in rats. Food and Chemical Toxicology 2010; 48:196–201.
94. Tibiri A, Banzouzi JT, Traore A, Nacoulma GO, Guissou IP, Mbatchi B. Toxicological assessment of methanolic stem bark and leaf extracts of *Entada africana* Guill. and Perr., Mimosaceae. International Journal of Pharmacology 2007; 3:393-99.
95. Udem SC, Obido O, Asuzu IU. Acute and chronic toxicity studies of *Erythrina senegalensis* DC stem bark extract in mice. Comparative Clinical Pathology 2010; 19:275-282.
96. Adedapo AA, Abatan MO, Idowu SO, Olorunsogo OO. Effects of chromatographic fractions of *Euphorbia hirta* on the rat serum biochemistry. African Journal of Biomedical Research 2005; 8:185-189.
97. Irene II and Iheanacho UA. Acute effect of administration of ethanol extracts of *Ficus exasperata* Vahl on kidney function in albino rats. Journal of Medicinal Plants Research 2007; 1:27-29.
98. Bafor EE and Igbinuwen O. Acute toxicity studies of the leaf extract of *Ficus exasperata* on haematological parameters, body weight and body temperature. Journal of Ethnopharmacology 2009; 123: 302-307.
99. Rasekh Hr, Nazari P, Nejad MK, Hosseinzadeh L. Acute and subchronic oral toxicity of *Galega officinalis* in rats. Journal of Ethnopharmacology 2008; 116, 21-26.
100. Santamaria LA, Ramirez G, Arellano AH, Zamilpa A, Jimenez JE, Cortes DA, Gutierrez EIC, Ledesma N, Tortoriello AH. Toxicological and cytotoxic evaluation of standardized extracts of *Galphimia glauca*. Journal of Ethnopharmacology 2007; 109: 35-40.
101. Qi Q. You Q, Gu H, Zhao L, Liu W, Guo Q. Studies on the toxicity of gambogic acid in rats. Journal of Ethnopharmacology 2008; 117:433-438.
102. Demma J, Gebre-Mariam T, Asres K. Toxicological study on *Glinus lotoides*: A traditionally used taenicidal herb in Ethiopia. Journal of Ethnopharmacology 2007; 111:451-457.
103. Rosidah, Yam MF, Sadikun A, Ahmad M, Akowuah GA, Asmawi MZ. Toxicology evaluation of standardized methanol extract of *Gynura procumbens*. Journal of Ethnopharmacology 2009; 123: 244-249.
104. Kumar G, Banu GS, Murugesan AG, Pandian MR. Preliminary toxicity and phytochemical studies of aqueous bark extract of *Helicteres isora* L. International Journal of Pharmacology 2007; 3: 96-100.
105. Pandey G. Acute toxicity of ipomeamarone, a phytotoxin isolated from the injured sweet potato. Pharmacognosy Magazine 2008; 4:S89-S92.
106. Li CY, Devappa RK, Liu JX, Lv JM, Makkar HPS, Becker K. Toxicity of *Jatropha curcas* phorbol esters in mice. Food and Chemical Toxicology 2010; 48:620-625.
107. Obici S, Otobone FJ, Sela VRS, Ishida K, Silva JC, Nakamura CV, Cortez DAG, Audi EA. Preliminary toxicity study of dichloromethane extract of *Kielmeyera coriacea* stems in mice and rats. Journal of Ethnopharmacology 2008; 115:131-139.
108. Hellion-Ibarrola MC, Ibarrola DA, Montalbetti Y, Villalba D, Heinichen O, Ferro EA. Acute toxicity and general pharmacological effect on central nervous system of the crude rhizome extract of *Kyllinga bervifolia* Rootb. Journal of Ethnopharmacology 1999; 66:271-276.
109. Khan A, Mosaddik MA, Rahman MM, Rahman MM, Haque ME, Jahan SS, Islam MS, Hasan S. Neuropharmacological effects of *Laportea crenulata* roots

in Mice. Journal of Applied Science Research 2007; 3:601-606.

110. Thanabhorn S, Jaijoy K, Thamaree S, Ingkaninan K, Panthong A. Acute and subacute toxicity study of the ethanol extract from *Lonicera japanica* Thunb. Journal of Ethnopharmacology 2006; 107:370-373.
111. Huang XH, Xiong PC, Xiong CM, Cai YL, Wei AH, Wang JP, Liang XF, Ruan JL. *In vitro* and *in vivo* antitumor activity of *Macrothelypteris torresiana* and its acute/subacute oral toxicity. Phytomedicine 2010; 17:930-934.
112. Karangwa C, Esters V, Frederich M, Tits M, Kadima JN, Damas J, Noirfalise A, Angenot L. Chemical and biological investigations of a toxic plant from Central Africa, *Magnistipula butayei* subsp. Montana. Journal of Ethnopharmacology 2006; 103:433-438.
113. Antia BS, Okokon JE, Nwidu LL, Jackson CL. Effect of sub-chronic adminitration of ethanolic stembark extract of *Mammea africana* Sabine on haematological and biochemical parameters of rats. African Journal of Biomedical Research 2006; 9:129-132.
114. Avancini SRP, Faccin GL, Vieira MA, Rovaris AA, Podesta R, Tramonte R, de Souza NMA, Amante ER. Cassava starch fermentation wastewater: Characterization and preliminary toxicological studies. Food and Chemical Toxicology 2007; 45:2273-2278.
115. Monjanel-Mouterde S, Traore F, Gasquet M, Dodero F, Delmas F, Ikoli JF, Lorec AM, Chamlian V, Portugal H, Balansard G, Pisano P. Lack of toxicity of hydroethanolic extract from *Mitragyna inermis* (Willd) O. Kuntze by gavage in the rat. Journal of Ethnopharmacology 2006; 103:319-326.
116. Harizal SN, Mansor SM, Hasnan J, Tharakan JKJ, Abdullah J. Acute toxicity study of the standardized methanolic extract of *Mitragyna speciosa* Korth in rodent. Journal of Ethnopharmacology 2010; 131: 404–409.
117. Mohan Kumari HP, Naidu KA, Vishwanatha S, Narasimhamurthy K, Vijayalakshmi G. Safety evaluation of *Monascus purpureus* red mould rice in albino rats. Food and Chemical Toxicology 2009; 47:1739-1746.
118. Adebajo AC, Ayoola OF, Iwalewa EO, Akindahunsi AA, Omisore NOA, Adewunmi CO, Adenowo TK. Anti-trichomonal, biochemical and toxicological activities of methanolic extract and some carbazole alkaloids isolated from the leaves of *Murraya koenigii* growing in Nigeria. Phytomedicine 2006; 13:246-254.
119. Adeneye AA, Ajagbonna OP, Adeleke TI, Bello SO (2006). Preliminary toxicity and phytochemical studies of the stem bark aqueous extract of *Musanga cecropioides* in rats. Journal of Ethnopharmacology 2006; 105: 374-379.
120. Tan PV, Mezui C, Orock GE, Njikam N, Dimo T, Bitolog P. Teratogenic effects, acute and sub chronic toxicity of the leaf aqueous extract of *Ocimum suave* Wild (Lamiaceae) in rats. Journal of Ethnopharmacology 2008; 115: 232-237.
121. Vaghasiya YK, Shukla VJ, Chanda SV. Acute oral toxicity study of *Pluchea arguta* Boiss extract in mice. Journal of Pharmacology and Toxicology 2011; 6:113-123.
122. Mukinda JT, Eagles PF. Acute and sub-chronic oral toxicity profiles of the aqueous extract of *Polygala fruticosa* in female mice and rats. Journal of Ethnopharmacology 2010; 123:236–240.
123. Chanda S, Dave R, Kaneria M, Shukla V. Acute oral toxicity of *Polyalthia longifolia* var. pendula leaf extract in wistar albino rats. Pharmaceutical Biology 2012; 50:1408-1415
124. Chavalittumrong P, Chivapat S, Attawish A, Bansiddhi J, Phadungpat S, Chaorai B, Butraporn R. Chronic toxicity study of *Portulaca grandiflora* Hook. Journal of Ethnopharmacology 2004; 90:375-380.
125. Barros S, Ropke CD, Sawada TCH, da Silva VV, Pereira SMM, de MoraesBarros SB. Assessment of acute and subchronic oral toxicity of ethanolic extract of *Pothomorphe umbellata* L. Miq (Pariparoba). Revista Brasileira de Farmácia 2005; 41:53-61.
126. Flammang AM, Erexson GL, Mirwald JM, Henwood SM. Toxicological and cytogenetic assessment of a Salacia oblonga extract in a rat subchronic study. Food and Chemical Toxicology 2007; 45:1954-1962.
127. Li X, Luo Y, Wang L, Li Y, Shi Y, Cui Y, Xue M. Acute and subacute toxicity of ethanol extracts from *Salvia przewalskii* Maxim in rodents. Journal of Ethnopharmacology 2010; 131:110-115.
128. Ramirez JH, Palacios M, Tamayo O, Jaramillo R, Gutierrez O. Acute and subacute toxicity of *Salvia scutellarioides* in mice and rats. Journal of Ethnopharmacology 2007; 109: 348-353.
129. Ferrero A, Minetti A, Bras C, Zanetti N. Acute and subacute toxicity evaluation of ethanolic extract from fruits of *Schinus molle* in rats. Journal of Ethnopharmacology 2007; 113: 441-447.
130. Lima LB, Vasconcelos CFB, Maranhão HML, Leite VR, Ferreira PA, Andrade BA, Araújo EL, Xavier HS, Lafayette SSL, Wanderley AG. Acute and subacute toxicity of *Schinus terebinthifolius* bark extract. Journal of Ethnopharmacology 2009; 126:468-473.
131. Choudhari CV, Deshmukh PB. Acute and subchronic toxicity study of *Semecarpus anacardium* on haemoglobin percent and RBC count of male albino rat. Journal of Herbal Medicine and Toxicology 2007; 1: 43-45.
132. Pieme CA, Penlap VN, Nkegoum B, Taziebou CL, Tekwu EM, Etoa FX, Ngongang J. Evaluation of acute and subacute toxicities of aqueous ethanolic extract of leaves of *Senna alata* (L.) Roxb. (Ceasalpiniaceae). African Journal of Biotechnology 2006; 5: 283-289.
133. Franco CIF, Morais LCSL, Junior LJQ, Almeida RN, Antoniolli AR. CNS pharmacological effects of the hydroalcoholic extract of *Sida cordifolia* L. leaves. Journal of Ethnopharmacology 2005; 98: 275-279.
134. Assam JP, Dzoyem JP, Pieme CA, Penlap VB. *In vitro* antibacterial activity and acute toxicity studies of aqueous-methanol extract of *Sida rhombifolia* Linn. (Malvaceae). BMC Complimentary and Alternative Medicine 2010; 10: 40.
135. Nwafor PA, Ekpo M, Udezi TW, Okokon J, Bassey AL. Acute toxicity potential of methanolic extract of Smilax kraussiana leaves in rats. International Journal of Pharmacology 2006; 2:463-466.
136. Akanmu MA, Olayiwola G, Ukponmwan OE, Honda K. Acute toxicity and sleep-wake eeg analysis of *stachtarpheta cayennensis* (Verbenaceae) in rodents. African Journal of Traditional and Complementary and Alternative Medicine 2005; 2: 222-232.
137. Kiendrebeogo M, Dijoux-Franca MG, Lamien CE, Meda A, Wouessidjewe D, Nacoulma OG. Acute toxicity and antioxidant property of *Striga hermonthica* (Del.) Benth (Scrophulariaceae). African Journal of Biotechnology 2005; 4:919-922.
138. Sanmugapriya E, Venkataraman S (2006). Toxicological investigations on *Strychnos potatorum* Linn. seeds in experimental animal models. Journal of Health Science 2006; 52:339-343.

139. Rebecca MA, Ishii-Iwamoto EL, Grespan R, Cuman RKN, Caparroz-Assef SM, de Mello JCP, Bersani-Amado CA. Toxicological studies on *Stryphnodendron adstringens*. Journal of Ethnopharmacology 2002; 83:101-104.
140. Ugbabe GE, Ezeunala MN, Edmond IN, Apev J, Salawu OA. Preliminary phytochemical, antimicrobial and acute toxicity studies of the stem, bark and the leaves of a cultivated *Syzygium cumini* Linn. (Family: Myrtaceae) in Nigeria. African Journal of Biotechnology 2010; 9: 6943-6947.
141. Kumar A, Padmanabhan N, Krishnan MRV. Centralnervous system activity of *Syzygium cumini* seed. Pakistan Journal of Nutrition 2007; 6: 698-700.
142. Abukakar MG, Ukwuani AN, Shehu RA. An evaluation of the toxic effects of *Tamarindus indica* pulp extract in albino rats. Journal of Pharmacology and Toxicology 2008; 3:111-3118.
143. Lahlou S, Israili ZH, Lyoussi B. Acute and chronic toxicity of a lyophilised aqueous extract of *Tanacetum vulgare* leaves in rodents. Journal of Ethnopharmacology 2008; 117: 221-227.
144. Odesanmi SO, Lawal RA, Ojokuku SA. Haematological effects of ethanolic fruit extract of *Tetrapleura tetraptera* in male dutch white rabbits. Research Journal of Medicinal Plants 2010; 4:213-217.
145. Adebayo JO, Balogun EA, Oyeleke SA. Toxicity study of the aqueous extract of *Tithonia diversifolia* leaves using selected biochemical parameters in rats. Pharmacognosy Research 2009; 1: 143-147.
146. Oyewole IO, Magaji ZJ, Awoyinka OA (2007). Biochemical and toxicological studies of aqueous extract of *Tithonia diversifolia* (Hemsl.) leaves in Wistar albino rats. Journal of Medicinal Plants Research 2007; 1: 30-33.
147. Liao JW, Chung YC, Yeh JY, Lin YC, Lin YG, Wu SM, Chan YC. Safety evaluation of water extracts of *Toona sinensis* Roemor leaf. Food and Chemical Toxicology 2007; 45: 1393-1399.
148. Akah PA, Alemji JA, Salawu OA, Okoye TC, Offiah NV. Effects of *Vernonia amygdalina* on biochemical and hematological parameters in diabetic rats. Asian Journal of Medical Sciences 2009; 1:108-113.
149. Monteiro MHD, Carneiro MRG, Felzenszwalb I, Chahoud I, Paumgartten FJR. Toxicological evaluation of a tea from leaves of *Vernonia condensata*. Journal of Ethnopharmacology 2001; 74: 149-157.
150. Ibrahim MY, Abdul ABH, Ibrahim TAT, Abdelwahab SI, Elhassan MM, Syam MM. Evaluation of acute toxicity and the effect of single injected doses of zerumbone on the kidney and liver functions in Sprague Dawley rats. African Journal of Biotechology 2010; 9:4442-4450.

How to cite this article:
Chanda S, Parekh J, Vaghasiya Y, Dave R Baravalia Y and Nair R: A Review: Medicinal Plants - From Traditional Use to Toxicity Assessment. Int J Pharm Sci Res 2015; 6(7): 2652-70.doi: 10.13040/IJPSR.0975-8232.6(7).2652-70.