

Toxic effects of some medicinal plants used in Moroccan traditional medicine

Mohamed Bnouham^{1*}, Fatima Zahra Merhfour¹, Mostafa Elachoui¹, Abdelkhaleq Legssyer¹, Hassane Mekhfi¹, Driss Lamnaouer² & Abderrahim Ziyat¹

¹Laboratoire de Physiologie et Ethnopharmacologie. Département de Biologie. Faculté des Sciences. Université Mohamed I^{er}. B.P. 717 - Oujda, Morocco. Tel: ++21267627496. Fax: ++2123650 06 03

²Institut Agronomique et Veterinaire Hassan II, Département de Pharmacie Toxicologie et Biochimie, Rabat-Instituts, Maroc.

Abstract

Phytoremedies are becoming mainstream worldwide; the increasing of these medicinal approaches is due to the recognition of the value of traditional medicine and indigenous pharmacopoeia. Although medicinal plants are often promoted as natural and therefore harmless, they are not free from adverse effects. The potential toxicity of herbal medicine is not new. In several countries, where herbal medicines are commonly used, it is well known that some plants must be used with caution because the adverse reaction can be caused inherently by toxic herbs, by herb overdoses, or by drug-drug interaction, thus, especially other adverse reactions can be due to quality problems such as adulteration caused by manufacturing, misidentification, substitution of one herb for another, improper processing of preparation and use, etc...

The present study reviews the cases of some plants commonly used by Moroccan people in traditional medicine and reported as highly toxic. Twenty-eight plants are selected as dangerous for health; these toxic species belonging to 16 families have been repertoried. The families reported to be most representative of these kinds of plants are Solanaceae (7 species). All physiological functions can be affected by the toxicity of plants. However, the highly toxic plants reviewed are those which produce irreversible health injury, serious aftermath, and irreversible damage such as renal failure, liver damage, hemiplegia, blindness...etc and sometimes they can produce death. The plants that have been reported to produce the severe damages are: *Aconitum vulparia* Rchb., *Anagyris foetida* L., *Atractylis gummifera* L., *Bryonia dioica* Jacq, *Chenopodium album* L., *Colchicum autumnale* L., *Conium maculatum* L., *Daphne gnidium* L., *Daphne laureola* L., *Ferula communis* L., *Hyoscyamus niger* L., *Mandragora autumnalis* Bertol, *Nerium oleander* L., *Ricinus communis* L., *Solanum nigrum* L., *Tamus communis* L. and *Thapsia garganica* L.

The review indicates the scientific name of the plant (family and species), the vernacular name, the part used, the LD50 (lethal dose 50) and summarized the most relevant toxicological investigations. The products carrying the toxicity of the plants and the acute toxicity have been mentioned. The great part of these toxic drugs belongs to the alkaloid class.

Key words: Toxic plants, Active components, Toxicity, Traditional medicine.

Introduction

The use of herbal medicines has increased considerably over the last decade over the world. Widespread reliance on traditional medicine can be attributed to 1) High cost of conventional medicine; 2) The belief that

herbal remedies are innocuous in contrast to conventional drugs; 3) The idea that what is natural can only be good; 4) The development of new diseases with severe complications, for which there is still no appropriate treatment and 5) The belief that herbal medicines are natural and safe.

* Corresponding author: Pr. Mohamed Bnouham
E-mail address: mbnouham@yahoo.fr

Although phytotherapy continues to be a main strategy of remedies in several countries, few plants received scientific or medical scrutiny (Gray and Flatt, 1998). Moreover, a high number of the medicinal plants possess a degree of toxicity. For example, it was reported that about one third of medicinal plants used in the treatment of diabetes are considered to be toxic (Marles and Fransworth, 1988).

This review is based on the literature such as using Medline and other reference sources materials including the books, the Moroccan thesis, the papers and reviews published in scientific journals and websites (such as FDA database and Cornell Poisonous plants) giving database on ethnobotanic, phytotherapy and toxicology. The Medline search included the following key words: herbs, herbal, traditional medicines, phytoremedies, toxicity, adverse effects, adverse reaction, drug-drug herbs interaction, overdose. In order to clarify this field for the scientific researchers as well as for the herbalists and users, we focused our searches only on the highly toxic plants commonly used by Moroccan people in traditional medicine in order to better highlight this field and to provide guideline for plant medicines users as for the herbalists, practitioners and consumers.

In this view we listed twenty seven plants more dangerous if they don't used carefully. These plants are those which produce irreversible health injury, serious aftermath, and irreversible damage such as renal failure, liver damage, hemiplegia, blindness...etc and sometimes they can produce the death.

Indeed, the list is best used only as a preliminary screening of potentially poisonous plants, not as a definitive conclusion of toxicity and a complete list of toxic plants.

Discussion

Several toxic plants (used with adequate amounts in traditional medicine) were useful for humanity during many centuries for the treatment of certain serious illnesses.

The colchicine, which is a highly toxic drug, obtained from *Colchicum autumnale* was very useful against congestive heart failure. The digitalin obtained from digital known for its high toxicity was very useful for the treatment of cardiac insufficiencies. In the same way we know very well the diverse important medical applications of the narcotics obtained from very toxic plants. These sorts of applications concern for example the belladonna that has a remarkable importance in pharmaceutical industry. Indeed, it intervenes in the manufacture of 86 drugs; that is to say, 10.42 % of pharmaceutical product in Morocco (Choulli et al. 1999). Although the seeds of *Citrullus colocynthis* are highly toxic, they were used for the treatment of diabetes. Recently, it has been shown that this plant contains insulinotropic compound (Abdel-Hassan et al. 2000. Nmila et al. 2000). The toxicity (acute toxicity) of some of these plants was largely highlighted. In Morocco, it was noted that a great number of intoxication cases in the Moroccan Poison Center (CAPM) are due to ingestion of the plants and products of traditional pharmacopoeia (2.5 % of the declared cases of intoxications) (CAPM). The most fatal toxic products in Morocco are the plants and the products of the traditional pharmacopoeia whose lethality reached 17 %. CAPM has registered 100 cases of intoxication by *Atractylis gummifera* between 1992 and 2000; that is to say 87.7 % of the total number of the registered cases (CAPM).

Since intoxications by *Atractylis gummifera* L. frequently happens in Morocco, this plant was relatively well studied in Morocco. Several tens of case of accidents due to the intoxication by *Atractylis gummifera* were studied and published (Berrada 1979, Sandali 1970). These studies made it possible to draw a clinical table related to the ingestion of *Atractylis gummifera*. This table includes a phase of latency of 24 H to 48 H before the appearance of the first signs of the intoxication. There is initially appearance of the digestive disorders then respiratory, cardiovascular disorders, and hepato-renal function disorders.

Table 1. Presentation of some plants used in Moroccan traditional medicine, their scientific names, the family, the vernacular name, the used parts, and information about medicinal uses, toxic components and toxicological signs

Scientific names Species names Family names	Local vernacular names	Used part	Medicinal uses	Toxics compounds	Toxicological signs	DL50 (mg/kg)	References
<i>Aconitum vulparia</i> Renonculaceae	- Ijantar -Quatel ed-dib - Hanq ed-dib	Root	Analgesic; Antirheumatic; Anticongestif; Against sciatic and teeth pain	- Aconitine	Vertigo; Diarrhea; Hypertension; Shivering Tachycardia; Respiratory paralysis	Iv cat 0,07-0,13 Iv rat 0,08-0,14 Or rat 1 Iv mouse 0,12 Sc mouse 0,27 Ip mouse 0,38 Or mouse 1,8	9,12,19
<i>Adonis oestivalis</i> Renonculaceae	- Ayn el hajla - Benaaman saghir - Dem elatrouss - Tit ntacknout	Leaves Stems	Sedative; Diuretic; Antirheumatic; Against asthma; Against epilepsy; Emenagogue	- Aconitic acid - Adonitol (ribitol) - Vernadin (coumarin)	Colic; Convulsion; Dyspnea; Hypertension	Ip rat >100 Iv mouse 180	4, 8, 20, 26, 31
<i>Anagyris foetida</i> Legumineuse	- Rharoub lkhenzir - Ful lkleb - Ufni ufen - Kharaya - Tizzat	Seeds	Against eczema; Purgative; Against renal disease; Emetic	- Anagyryne (alkaloid)	Tachycardia; Hypertension; Vomiting; Diarrhea		4, 20
<i>Aristolochia longa</i> Aristolochiaceae	- Breztom - Chajrat rustom - Qitte lehmir lberi - Aarifi - Ajrachi	Roots	Against intestinal pain; Diuretic; Cutaneous diseases; Cataplasma against snake	Aristolochic acid	Nephrotoxicity; Carcinogenic effects; Alteration of liver and kidney enzymes; Damage liver and kidney	Or rat 184-203 Iv mouse 22,4 Or mouse 49-106	4, 8, 12, 25
<i>Atractylis gummifera</i> Compositae	- Addad - Ahfyun - Ishis	Roots	Emetic	Diterpenic heterosides : atractylosides, carboxyatractylosides, parquaine, carboxiparquaine	Death	- Iv rat 431 -Ip mouse 580	6, 12, 20

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<i>Atropa belladonna</i> Solanaceae	- Zbib elkhidus - Tidilla - Aadil wussen - Buquinin	Roots Leaves	Narcotic; Diuretic; Antispasmodic; Treatment of eye diseases; Antidote of opium; As lotion; Rheumatism and sciatic; Giving in collapse of pneumonia; Typhoid fever	- Troponic acid ester - Tropanol (scopariol) - Atropine - Hyosциamine (alkaloid) - Scaplomine - Starch - Belladonine (apoptropine)	Nervous system intoxication	Or rat 750 Sc rat 3800 Iv rat 170 Iv mouse 153 Sc mouse 590-1700 Iv mouse 400 Iv rabbit	6, 12, 18, 20, 34
<i>Bryonia dioica</i> Cucurbitaceae	- Luwaya - Fasir - Kerma elbayda - Herbuna	Roots Fruits	Against dysentery; Purgative; Against ulcer	- Cucurbitacin (tetracyclic diterpen) - Brydiofin	Titanic convulsion; Hypothermia; Cramp; Coma	Or mouse 340	4, 12, 20 23
<i>Chenopodium album</i> Chenopodiaceae	- Blis - Remrem, beremrem - Blitu	Roots	Against colic	- Oxalic acid	Trouble of CNS; Cephalgia; Vertigo; Paralysis; Nausea; Vomiting; Hypotension with meningitis	LDlo, Or human 700 - 30,000 ppm	3, 12, 20, 29, 35
<i>Citrullus colocynthis</i> Cucurbitaceae	- Hantal - Lehdej - Umheddijit - Alkad - Aaknet - Lemnun serqui	Fruits Seeds	Antidiabetic; Against blenorrrhagia	- Elateridine - Glycosides - Resin - Dihydric alcohol - Heliacontane - Citrullin - Citrullinic acid	Gastrointestinal pain; Diarrhea; Vomiting; Hypothermia; Cardiac disorder; Cerebral congestion; Necrosis of liver and renal cells	2500	8, 11, 20, 27
<i>Colchicum autumnal</i> Liliaceae	- Bukbuka - Elbsila - Tirket	Seeds Capsule	For rheumatism; Arthritis; Sedative; Act upon all secreting organs particularly the bowels and kidneys	Colchicine (alkaline substances)	Vomiting; Diarrhea; Antimitotic; General paralysis; Respiratory paralysis		18, 19
<i>Conium maculatum</i> Compositae	- Sikran - Barbus - Ziyayata	Whole plant	Narcotic; Sedative; Antispasmodic; Antidote of strychnine; Tetanus;	- Coniine (alkaloid) - Conhydrine - Methyl coniine	Asphyxia; Death	Or mouse 100 Sc mouse 80 Iv rabbit LDlo 15	8, 18, 20

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	- Banj		Hydrophobia; Spasm of larynx; Gullet; Asthma; Cure tumors; Swilling and pains of the joints and skin	- Pseudoconhydrine - Ethyl piperidine - Mucilage - Fixed oils		Sc rabbit LD ₅₀ 80	
<i>Daphne gnidium L</i> Thymelaceae	- Lezzar - Metnan - Inif	leaves	Hair care; Against tinea	- Tannin - Vesicant resin - Daphnetoxin - Mezerin	Headache, Shivering, Paleness; Pupil dilation; Diarrhea; Convulsion; Pulmonary disorder; Difficulty of deglutition; Death;	Or UnK 0,25	4, 6, 8, 12, 20, 27
<i>Daphne laureola</i> Thmeleaceae	- Ad-dufayla - Talidrar - Walidrar	leaves	Laxative; Strong purgative	Berries	Paleness; Pupil dilation; Mouth and lips swelling; Diarrhea; Convulsion; Pulmonary disorder; Difficulty of deglutition; Death		4
<i>Datura stramonium</i> Solanaceae	- Chdeq ejjmel - Taburzigt - Tidila - Ghayata - Elmurquid - Jawzat elmurquid - almuswika	leaves	Antispasmodic; Emollient; Narcotic; Against asthma; Palliate the pain; Muscle rheumatism; Neuralgia; Hemorrhoid; Fistula; Abscesses; Inflammation	-Hyosциamine(alkaloide) - Atropine - Hyoscine (scopolamine) - Malic acid - Daturin (mixture of hyosциamine and atropine)	Serious neuralgic; Hallucination		18, 20
<i>Diditalis purpura</i> Scrofulariaceae		Leaves	Diuretic; Cardiotonic; For cardiac arrhythmias oedema; Oliguria	- Digitalis - Glycosides - Digtosin - Digitalin - Digitalein - Digitonin	Cardiovascular, neurological and digestive troubles; Hallucination; Photophobia; Exophthalmia		18, 19
<i>Ferula communis</i> Apiaceae	Ikelha; Ufful, tuffat; Anbi, auli; Tagult; I-bubal	Resine	Antidiabetic; Sedative	4 hydroxy coumarinic; ferulic, hydroxyferulic, hydroxyfelinol, hydroxyfelinol, hydroxyfelinol, hydroxyfelinol,	Hypoprothrombinuria; Hemorrhage (internal and external); Anti vitamin K;	Or rat 1650 Or mice 2g/kg	4, 13, 15, 16, 20, 33

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<i>Hyoscyamus niger</i> Solanaceae	Sikran; Bunarijuf; Benj; Lebтина, Gengit; Afelhelhe; Falezlez; Barbar	Resine	Against spinal column	ferprenine and isoferprenine - Alkaloids, hyociamine, atropine, scopolamine	Anorexia; Diarrhea; Hypothermia; Weakness Convulsion; Dyspnea; Digestive disorder; Vegetative nervous disorder; Tachycardia; Dryness of mucus membrane; Cardiac depression; Coma and death	Iv mouse 95	20
<i>Iris pseudoacorus</i> Iridaceae	- Ud alambar - Ambar - Sif ed-dib - Sekkin eddib - Busrika	Rhizome	Emetic; Purgative; Rubefacient Against sneezing	- Irisin - Iridin	Abdominal pain; Nausea- Vomiting; Diarrhea; Spasm; Staggering; Paralysis		20
<i>Mandragora autumnalis</i> Solanaceae	- Bid elghoul - Taryala - Luffah - Ybruh - Luffah eljenn	Roots Leaves	Against asthma and cold; Narcotic; Anesthetic; Apetizine	- Atropine - Hyoscyamine - Scopolamine	Death		4, 27
<i>Nerium oleander</i> Apocinaceae	- Ddefla - Elel - lili	Leaves	Hypoglycemic; Against headache	- Oleandrin - Nerine (neroside) - Oleandroside - Ouabain - Cardiotoxics - Digitoxine	Vomiting; Shivering; Gastroenteritis; Respiratory disorder; Death by asphyxia; Weakness; Bradycardia; Convulsion; Hyperthermia; Heart failure	Iv cat 0,3 Nerium LDlo sc mouse 95	4, 6, 8, 12, 19, 20, 37
<i>Ricinus communis</i> Euphorbiaceae	- Kherwaa - Krank - Tmazzit - Awriys	Seeds	Against sterility; For hair	- Ricin	Death	Iv rat 500 ng/kg Parenteral rat 326 ng/kg Or rat Ldllo 30	4, 20

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<i>Solanum nigrum</i> Solanaceae	- Ineb eddib - Ineb ettaaleb - Buqina - Adilwussen	Leaves	Emolient; Antineuralgic; Sedative; Strong sudorific; Promotes sleep for infant; Cutaneous disorders; Burns; Ulcers; Gout	- Solanine - Solanidine	Narcotic properties; Vomiting; Cephalia mental confusion; Tachycardia; Hallucination; Coma; Death; Potential CNS depressant action	Sc mouse 22,1 If mouse 2 µg/kg Iv mouse 2,2 µg/kg Or man 300 µg/kg Sc man Ldlo 43 µg/kg Or man Ldlo 900 µg/kg	4, 18, 22
<i>Solanum sodomaeum</i> Solanaceae	- lim nsara - Hedja - Mtisat lehmir	Leaves	For eye cleaning; Stopping the menses; Aphrodisiac; Against insomnia	- Glucoalkaloids (heterosides of solasodine) - Saponosides			4, 20, 27
<i>Tamus communis</i> Dioscoreaceae	- Tamier - Belmimoune	Leaves Stem	- Against skin diseases - Against rheumatism and lumbago; Rubifacient; Diuretic; For asthma complaints; Stimulating plaster	- Campestrol - Stigmastrol - β sistrol	Irritation of the mucous membrane; Trouble of respiration	Ip mouse 3 Inj rat LDlo 10	12, 18, 20
<i>Taxus baccata</i> Taxaceae	- Dahs - Igen - Adgan - Imerwel	Leaves	Treatment of rheumatism	-Cyclitols; -Fatty acid; - Stérols - bisflavonoids - ProanthoCyanidols - Lignanes -Cyanogenetic Heterosides; -Terpens	Paralysis of cardiac and pulmonary functions; Hypotension; Respiration depression; Vomiting; Nausea; Diarrhea; Abdominal pain; Convulsion; Coma		4, 19, 20, 27

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<i>Thapsia garganica</i> Compositae	- Deryas - Bu-neffaa - Tufflet - Alauu - Usbat anissa	Roots	Against rheumatism; Bronchitis; Feminine sterility	Resin	Vomiting; Violent diarrhea; Digestive mucous inflammation; Salivary secretion; Nervous disorder; Violent colic; Gastroenteritis; Death	4, 8, 20	
<i>Urginea maritima</i> Liliaceae	- Bsal alfar - Bsal elkhenzir - Dsal elferawn - Ferruma - Azalim u wussen - Ikfil - Isquif	Bulb	Against sterility; For mouth care	Bitter and corrosive juice		20	
<i>Withania somnifera</i> Solanaceae	- Hab al lahw - Sikran - Ineb eddib - Sem elfar	Seeds Roots	Narcotic; Sedative; Antiepileptic; Diuretic; Light laxative; Abortive	Alkaloids	Vomiting; Tetanic convulsion; Mydriasis	4, 27	

Abbreviations: **iv:** intra venous; **sc.:** sub cutaneous; **im:** intra muscular; **or:** oral; **LD50:** lethal dose 50; **LDLo:** Lethal dose low; the lowest dose in an animal study at which lethality occurs. **FDA:** U. S Food and drug administration; **ip:** intraperitoneal; **WHO:** World Health Organization; **CAPM:** Anti-Poisonous Moroccan Center. **Unk:** unknown.

References: 1. Abadome, 1988; 2. Abdel-Hassan et al. 2000; 3. Bellakhdar, 1978; 4. Bellakhdar, 1997; 5. Berrada; 1979; 6. Bruneton, 1996; 7. CAPM: Centre AntiPoison Maroc; 8. Charnot; 1945; 9. Choulli et al. 1999; 10. Cornell Poisonous plants; 11. Diwan et al. 2000; 12. Duke, 1992; 13. El Alouani, 1986; 14. FDA; U. S Food and drug administration; 15. Fraigui et al. 2001; 16. Fraigui et al. 2002; 17. Gray & Flatt; 1998; 18. Grieve; 1971; 19. Hmamouchi, 1999; 20. Kahouaji; 1995; 21. Marles & Fransworth 1988; 22. Merck Index 12th edition. Merck and Co INC. 1996; 23. Munoz et al. 1992; 24. Nimla et al. 2000; 25. Pakrashi & Shaha, 1979; 26. Palevitch, 1982; 27. Paris & Moyse, 1976-1981; 28. Perez et al. 1998; 29. Rahmani, 1979; 30. Sandali, 1970; 31. Sharma et al. 1978; 32. Skalli et al. 2002; 33. Tligui et al. 1994; 34. Trabattoni et al. 1984; 35. Whitehead & Moxon, 1952; 36. World Health Organization Expert Committee on Diabetes Mellitus; 1980; 37. Ziyayat et al., 1997

Finally a hepatic coma and death occurs 4 to 6 days after ingestion of *Atractylis*. In order to take stock of this intoxication of which diagnosis is clinical and treatment symptomatic, Skalli et al. in 2000 have suggested analyzing one clinical case of the intoxication by *Atractylis gummifera* L. on a 12 year old child who accidentally ingested this plant. In fact, the sweetened taste of the root of this plant especially facilitates the intoxication in the child (Bellakhdar, 1997).

The intoxication by seeds of *Ricinus communis* can be accidental. The seeds of the fruits of *Ricinus communis* are frequently confused with edible seeds. The intoxication can occur by therapeutic overdose or following their use as abortive. Bellakhdar in 1997 reported that intoxication has been produced in Goulimine (southern of Morocco) following a traditional treatment against female sterility consisting of the *Ricinus communis* seed ingestion associated with a vaginal rectal injection with a solute of seed decoction. The castor seeds are often used like abortive (Bellakhdar, 1997).

The intoxications by another toxic plant: *Ferula communis* are well known in Morocco as well for the animals as for the Man. It is a plant which was much studied. The toxic principle of this plant is concentrated in secretions which give a product locally called "Fessoukh". This product is not water soluble and hexane but it is soluble in the acetone, the chloroform and solution of NaOH (3 %) (El Alouani, 1986). It has been tried to profit to prepare rodenticide from *Ferula communis*

(Abadome, 1988). Moreover, a trial conducted with wild rats using 0.1 % "Fessoukh" extract baits demonstrated "Fessoukh" rodenticide effects (Fraigui et al. 2001).

The most toxic plants listed in this review are 28 species belonging to 16 families. The familie that have been reported to be most representative of the highly toxic plants used in the traditional medicine in Morocco is Solanaceae (7 species).

A great part of the poisonous substances of the plants listed in this review belongs to the class of alkaloids. It is the case of the following plants: *Aconitum vulparia*, *Anagysis foetida*, *Atropa belladonna*, *Conium maculatum*, *Datura stramonium*, *Digitalis purpurea*, *Hyosciamus niger*, *Mandragora autumnalis*, *Withania somnifera*.

In conclusion, the families most representative of these plants are the family of Solanaceae (7 species). The intoxication by these plants is not only related to the fact that they are used in traditional herbal medicine but more especially because of some factors such as: the overdose, bad methods of use as well as confusion with other edible plants. The children are touched the most by these intoxications. The majority class of the toxic principles of these plants belongs to alkaloids. Moreover, strong efforts are wished to inform populations that continue to use traditional medicine in order to avoid the bad practices due to the ignorance of the good uses of the traditional medicine.

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