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Pharmacological screening of some Brazilian plants

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Forty-five species of plants from several botanical families growing in North East Brazil have been examined for toxicity on mice and small fishes, cat blood pressure and respiration, isolated toad heart and rectus abdominis muscle, guinea-pig ileum, rabbit duodenum and rat uterus. A high toxicity to mice and fishes was exhibited by aqueous (A) and ethanolic (B) extracts from *Luffa operculata*, *Peschiera affinis*, *Pithecelobium multiflorum* (gall) and *Zizyphus joazeiro* and by extract B from *Pithecelobium multiflorum* (stem-bark). Cardiorespiratory activity was shown by *Annona squamosa*, *Byrsonima sericea*, *Crataeva tapia*, *Erythrina velutina*, *Fagara rhoifolia*, *Operculina macrocarpa*, *Perschiera affinis*, *Pithecelobium multiflorum*, *Spondias lutea* and *Zizyphus joazeiro*. Extracts A and B from *Operculina macrocarpa* and *Pithecelobium multiflorum*, extract A from *Luffa operculata* and *Zizyphus joazeiro* and extract B from *Crataeva tapia* and *Peschiera affinis* promoted a contraction of the toad rectus abdominis muscle. Both extracts from *Annona aquamosa* and *Fagara rhoifolia* (leaf) provoked a spasmogenic effect on guinea-pig ileum and a spasmolytic one on rabbit duodenum. Extracts A and B from *Pithecelobium multiflorum*, *Vitex gardneriana* and *Zizyphus joazeiro* exhibited a spasmogenic activity on both preparations, while extracts A and B from *Peschiera affinis* and extract B from *Erythrina velutina* also evidenced a spasmolytic activity on both preparations. Oxytocic activity was shown by both extracts from *Annona squamosa*, *Byrsonima sericea*, *Pithecelobium multiflorum* and *Vitex gardneriana*.

We have made a pharmacological examination of forty-five plant species growing in the neighbourhood of Fortaleza (Brazil) along similar lines to those adopted by Feng, Haynes & others (1962) in their examination of West Indian plants.

The tests were arranged according to Laurence & Bacharach (1964) and Turner (1965). The work was aimed at selecting interesting material for further study.

EXPERIMENTAL

Plant extractions

Botanically identified species were collected and processed immediately. Extracts were prepared by boiling the reduced part of the plant, on a water bath, in distilled water (extract A) or ethanol (extract B) filtering through calico and repeating the procedure with the residue. The filtrates were combined and evaporated. The final concentration of the extracts were adjusted to give the equivalent of 1 g material per ml of solvent. Where the viscosity was unsuitable for pharmacological experiments the concentration was adjusted to 1:10. Before use the ethanolic extract was evaporated on a water bath and its original volume made up with distilled water and neutralized with N sodium hydroxide when necessary and stored at 4°.

Pharmacological testing

The following tests were made on the extracts.

Acute toxicity in mice. Extracts A and B were given by intraperitoneal injection (0·1, 0·2, 0·4 and 0·8 ml) to groups of four adult mice of either sex and random strain. The minimum dose required to kill all animals of a group within 24 h was used as the toxic dose level (Table 1).

Acute toxicity in the fish Lebistes reticulatus. Ten fishes were placed in flasks containing 0·5 ml of the extracts in 300 ml of water and the lethality (%) after 24 h recorded. Water or water plus 0·5 ml of ethanol was used as a blank.

Cat respiration and blood pressure. Adult cats anaesthetized with pentobarbitone sodium (30 mg/kg, i.p.) were prepared for the measurement of respiratory movements and carotid blood pressure after being given heparin. After slow injection of extract (0·5–2·0 ml) through the femoral vein, pressor or depressor responses and stimulation or depression of respiration were noted (Table 1).

Toad rectus abdominis muscle preparation (Burn, 1952; Valle, 1955). Extracts (0·1–0·5 ml) enhancing the contraction of the muscle or antagonizing acetylcholine-induced contractions (up to 20 μg) were recorded (Table 1).

Toad heart preparation. The effects on heart rate, amplitude and rhythm were registered. Injections of extracts (0·1–0·5 ml) were made by a syringe through the polyethylene tube on the side arm of the perfusion cannula, containing 5 ml of frog-Ringer solution, tied in the inferior vena cava.

Guinea-pig ileum and rabbit duodenum in vitro. Pieces of gut were set up in a 10 ml bath containing aerated Tyrode solution at 37° to record the effect up to 0·5 ml of the extracts on the longitudinal muscle contractions (Burn, 1952). Acetylcholine (up to 10 μg) was used as control drug. The effects of extracts (0·1–0·5 ml) on tonus and motility of the rabbit duodenum were also noted (Table 1).

Rat uterus. A segment of uterus from an adult virgin rat pretreated with 10 μg of stilboestrol was suspended in a 10 ml bath containing the De Jalon solution and longitudinal contractions were recorded in the usual way. Oxytocin (0·001–0·01 i.u.) was used as control. The extracts (0·1–0·5 ml) were tested for their spasmogenic effect and also their ability to inhibit contractions induced by oxytocin.

RESULTS

The results are tabulated in Table 1. Among the species of plants we have studied a high level of toxicity was shown by extracts from *Krameria tomentosa* (root), *Luffa operculata*, *Peschiera affinis*, *Pithecelobium multiflorum* (gall), *Simaruba versicolor* (root-bark), *Triplaris gardneriana* and *Zizyphus joazeiro*. Whereas most extracts exhibited a depressor action upon the carotid blood pressure only the ethanolic extract of *Borreria verticilata* (overground portion) and *Fagara rhoifolia* and aqueous and ethanolic extract from *Delonix regia* exhibited a pressor action.

Nearly all the species studied were active on the cat respiration, and have stimulant or depressor effects.

Contraction of the toad rectus abdominis muscle was observed mainly after addition to the bath of aqueous and ethanolic extracts from *Operculina macrocarpa*, *Pithecelobium multiflorum* and *Zizyphus joazeiro*, aqueous extract from *Luffa operculata* and *Sapindus saponaria* and ethanolic extract from *Crataeva tapia*.

Table 1. *Pharmacological actions of aqueous extracts (A) and ethanolic extracts (B) of forty-five Brazilian plants*

Species, family, common usage name	Part used	Extract and concn used		Toxicity		Cat		Toad		G.P.	Rabbit duodenum		Rat
				Mice	Fish	B.P.	Resp.	Rect. abd.	Heart	ileum	Tonus	Motility	uterus
Alpinia speciosa Schum.	Leaf	A	1:1	O	O	O	O	O	D	+++	–	O	++
Zingiberaceae (Colônia)		B	1:1	O	O	O	O	O	D	+	—	–	– –
Anacardium occidentale L.	Tegument	A	1:3	O	100	D	D	O	D	+	–	O	+++
Anacardiaceae (Cajueiro)		B	1:1	†	100	D	S	++	D	+	–	O	– – –
Annona squamosa L.	Leaf	A	1:10	†††	O	D	S	O	S	+++	–	–	+++
Annonaceae (Ateira, Ata)		B	1:1	††	O	D	S	–	D	+++	–	–	+++
Boerhaavia coccinea Mill.	Root	A	1:1	†	O	O	S	O	S	+	+	O	+
Nyctaginaceae (Pega-pinto)		B	1:1	O	O	O	S	O	S	O	–	O	+
Borreria verticilata J. F. W. Mayer	Root	A	1:1	O	O	D	S	O	D	O	+	O	++
Rubiaceae (Vassourinha de botão)		B	1:1	O	O	O	O	O	D	O	+	–	++
	Overground portion	A	1:3	O	O	D	O	– –	D	++	–	–	+++
		B	1:1	O	O	P	S	– –	D	++	–	–	+++
Byrsonima sericea D.C.	Stem-bark	A	1:10	††	100	D	D	O	S	– –	+	O	+++
Malpiguiaceae (Murici-pitanga)		B	1:10	††	100	D	D	O	S	– –	+	O	+++
Cannabis sativa L. ♀	Flowering tops	A	1:2	†††	O	O	O	O	D	+	–	–	+++
Cannabinaceae (Maconha)		B	1:2	O	100	O	S	O	D	–	–	–	+++
Cecropia carbonaria Mart.	Leaf	A	1:1	†	O	D	O	O	D	– – –	–	–	+
Moraceae (Torém, Gargaúba)		B	1:1	†	O	D	O	O	D	– – –	–	–	++
Cochlospermum insigne St. Hill.	Stem-bark	A	1:2	††	O	O	O	O	D	++	–	O	++
Cochlospermaceae (Pacotê)		B	1:1	O	O	O	O	O	D	– –	–	O +	++
Cochlospermum vitifolium Spreng.	Stem-bark	A	1:1	†††	O	D	D	O	D	++	–	+	++
Cochlospermaceae (Algodão-bravo)		B	1:1	O	O	O	O	O	D	++	+	–	++
Coutarea hexandra Schum.	Stem-bark	A	1:1	†	10	D	O	– – –	D	+++	+	+	– – –
Rubiaceae (Quina-quina)		B	1:1	†	10	D	O	– –	D	– – –	–	–	– – –
Crataeva tapia L.	Leaf	A	1:5	O	O	D	S	+	D	+++	–	–	+++
Capparidaceae (Trapiá, tapiá)		B	1:5	O	O	D	S	+++	O	+++	+	O	O
	Stem-bark	A	1:1	O	O	D	S	+	O	+++	–	O O	O
		B	1:1	O	O	D	S	+++	O	+++	O	O	O
Curatella americana L.	Stem-bark	A	1:2	†††	O	O	O	–	S	O	–	O –	– –
Dileniaceae (Cajueiro-bravo)		B	1:1	††	100	D	O	– –	S	++	–	–	–
Delonix regia Raf.	Stem-bark	A	1:1	†††	O	P	S	O	S	+++	–	O	– –
Leguminosae papilionoideae (Flambuaiã)		B	1:1	†	O	P	S	O	D	+++	–	O –	++
Diodia barbeyana Hub.	Root	A	1:1	O	O	O	O	O	S	–	O	–	+
Rutaceae (Saca-estrepe)		B	1:1	O	O	D	D	O	S	– –	–	–	–
Erythrina velutina Wild.	Stem-bark	A	1:1	O	O	O	S	– –	S	+	–	–	+++
Leguminosae papilionoideae (Mulungu)		B	1:1	†	10	D	D	– – –	D	– – –	–	–	++
Fagara rhoifolia Engl.	Leaf	A	1:1	†	10	D	O	O	S	+++	–	–	–
Rutaceae (Limãozinho)		B	1:1	†	O	P	O	O	S	+++	–	–	–
	Stem-bark	A	1:1	O	O	O	O	O	S	O	–	–	– –
		B	1:1	†	O	P	O	++	S	+++	–	–	– –
Guazuma ulmifolia Lam.	Stem-bark	A	1:1	†	O	O	O	O	D	–	–	–	+
Sterculiaceae (Mutamba)		B	1:1	O	O	O	O	O	S	+	–	–	++
Guetarda angelica Mart.	Root-bark	A	1:2	†	O	O	S	O	O	–	–	O	++
Rubiaceae (Angélica)		B	1:1	††	O	D	S	O	O	– –	+	–	++
Heliotropium indicum L.	Root	A	1:1	†	O	D	O	O	D	O	+	O	+++
Borraginaceae (Fedegoso)		B	1:1	O	O	O	O	O	D	– –	–	O +	+++
Hymenaeae courbaril L.	Stem-bark	A	1:2	†††	O	D	D	O	D	O	+	–	– –
Leguminosae papilionoideae (Jatobá)		B	1:2	†	100	D	D	–	O	– – –	–	O –	– – –
Krameria tomentosa Mart.	Stem	A	1:10	†††	O	D	O	O	D	O	+	–	O
Leguminosae caesalpinoideae (Carrapicho)		B	1:10	††	20	D	O	O	D	–	+	O	O
	Leaf	A	1:10	††	100	D	S	–	D	– –	+	–	O
		B	1:10	††	100	D	O	–	D	– –	+	O	+

Table 1—*continued*

Krameria tomentosa	Root	A	1:1	†††	100	O	O	O	O	– –	O	O	–
		B	1:1	†††	100	D	S	O	D	– – –	O	O	– – –
Lagancularia racemosa Gaert.	Leaf	A	1:1	†††	70	D	S	O	D	–	–	–	
Combretaceae (Mangue branco)		B	1:1	†††	60	D	S	O	D	– –	–	–	–
Lantana camara L.	Root	A	1:1	††	O	D	S	O	S	O	+	O	O
Verbenaceae (Camará)		B	1:1	†	O	O	O	O	S	O	+	O	O
Luffa operculata Cogn.	Fruit	A	1:10	†††	90	O	S	+ + +	D	+	+	–	+
Cucurbitaceae (Cabacinha)		B	1:10	†††	100	O	S	+	D	+	+	–	+
Operculina macrocarpa Urban.	Tuber	A	1:2	†††	O	D	S	+ + +	D	+ +	+	–	+ +
Convolvulaceae (Batata de purga)		B	1:2	†††	O	D	S	+ + +	D	+ +	+	–	+ +
Peschiera affinis Miers.	Root-bark	A	1:1	†††	100	D	S	– –	D	– –	–	–	+
Apocinaceae (Grão-de-galo)		B	1:1	†††	100	D	S	+ + +	D	– –	–	–	+
Pithecelobium multiflorum Benth.	Stem-bark	A	1:1	†††	O	D	S	+ + +	D	+ + +	–	–	+ +
Leguminosae mimosoideae (Canafístula de boi)		B	1:1	†††	100	D	S	+ + +	D	+ +	+	–	+ + +
	Gall	A	1:2	†††	100	D	O	+ + +	D	+ + +	+	–	+ + +
		B	1:2	†††	100	D	O	+ + +	D	+ + +	+	–	+ + +
Plumeria bracteata A.D.C.	Root-bark	A	1:1	††	100	O	O	O	S	O	+	O	+
Apocinaceae (Janaguba)		B	1:1	O	100	O	O	O	S	O	+	O	+
Sapindus saponaria L.	Stem-bark	A	1:1	O	O	D	D	+ + +	D	+ + +	–	–	–
Sapindaceae (Sabonete)		B	1:1	O	O	O	D	O	S	+	+	O	– – –
Scoparia dulcis L.	Root	A	1:1	††	O	D	D	O	S	O	+	–	+
Scrophulariaceae (Vassourinha)		B	1:1	O	O	D	D	O	S	O	+	–	+
Simaruba versicolor St. Hill.	Stem-bark	A	1:5	†††	O	D	D	– –	S	– – –	–	–	– – –
Simarubaceae (Pau paraíba)		B	1:2	†	O	D	O	– – –	S	– – –	–	–	– – –
	Root-bark	A	1:1	†††	100	D	O	+ +	D	–	O	–	+
		B	1:1	†††	90	D	O	+	D	– –	–	–	+ +
Solanum paniculatum L.	Root	A	1:1	††	O	D	S	+	S	–	–	–	+
Solanaceae (Jurubeba)		B	1:1	†††	90	D	D	+	S	– –	–	–	+
Spondias lutea L.	Stem-bark	A	1:1	†	O	D	D	+ +	D	+ +	+	O	+ +
Anacardiaceae (Cajazeira)		B	1:1	†	100	D	D	O	D	+ +	+	+	+ + +
Strychnos parvifolia D.C.	Fruit	A	1:1	†	O	D	D	O	S	–	–	–	
Loganiaceae (Urari)		B	1:1	O	O	D	D	O	S	–	–	–	–
	Seed	A	1:1	†	O	D	D	O	S	+ +	–	O	–
		B	1:1	O	O	D	D	O	S	–	+	–	– – –
Tabebuia caraiba Mart.	Stem-bark	A	1:1	††	O	D	D	+ +	D	–	–	–	–
Bignoniaceae (Caraúba)		B	1:1	††	O	D	D	O	D	– – –	–	–	– –
Talisia esculenta Radlk.	Stem-bark	A	1:1	†	O	D	S	O	D	+ +	–	O	O
Sapindaceae (Pitombeira)		B	1:1	O	O	D	D	O	O	+ +	O	O	O
Tapirira guyanensis Aubl.	Stem-bark	A	1:1	†††	100	D	D	+	S	O	+	O	+ +
Anacardiaceae (Pau-pombo)		B	1:2	O	100	D	D	–	S	O	+	O	+
Tocoyema formosa Schum.	Root-bark	A	1:1	†	O	D	D	O	S	O	+	O	+ + +
Rubiaceae (Jenipapo-bravo)		B	1:1	†	O	O	D	O	D	O	–	O	– –
Triplaris gardneriana Wild.	Stem-bark	A	1:2	††	100	D	D	O	S	+	+	O	+ +
Poligonaceae (Pajeú)		B	1:2	†††	100	D	O	O	S	+ +	+	O	+ + +
Turnera sp.	Root	A	1:1	†	O	D	S	O	D	–	–	–	+
Turneraceae (Chanana)		B	1:1	O	O	D	S	O	D	O	–	O	+ + +
Vitex gardneriana Schau.	Stem-bark	A	1:1	†	O	D	O	+ +	D	+ + +	+	–	+ + +
Verbenaceae (Tarumã)		B	1:1	O	O	D	D	O	D	+ + +	+	–	+ + +
Wilbrandia sp.	Tuber	A	1:1	††	100	D	O	–	S	–	+	+	+
Cucurbitaceae (Cabeça-de-negro)		B	1:1	††	70	D	D	–	S	–	–	–	–
Zizyphus joazeiro Mart.	Stem-bark	A	1:1	†††	100	D	S	+ + +	S	+ + +	+	+	+
Ramnaceae (Juàzeiro)		B	1:1	†††	100	D	S	+ +	S	+ + +	+	–	+ +
Zizyphus undulata Reiss.	Stem-bark	A	1:1	††	40	D	S	+ +	D	+ + +	+	+	+ + +
Ramnaceae (Juamirim)		B	1:1	†	O	O	O	O	S	+ +	–	O	+ +

A = aqueous extract
B = ethanolic extract
† = degree of toxicity

number = death per cent
D = depressor effect
P = pressor effect

S = stimulant effect
+ = stimulant effect
– = inhibition.

O = no effect

Most extracts showed a depressor effect on toad heart, however extracts from *Boerhaavia coccinea*, *Byrsonima sericea*, *Curatella americana*, *Diodia barbeyana*, *Fagara rhoifolia*, *Lantana camara*, *Plumeria bracteata*, *Scoparia dulcis*, *Solanum paniculatum*, *Strychnos parvifolia*, *Tapirira guyanensis*, *Triplairis gardneriana*, *Willbrandia* sp. and *Zizyphus joazeiro* showed a stimulant effect.

Whereas extracts from *Cecropia carbonaria* (leaf) and *Simaruba versicolor* did exhibit a spasmolytic action upon guinea-pig ileum and rabbit duodenum, extracts from *Annona squamosa*, *Delonix regia* and *Fagara rhoifolia* (leaf) provoked a spasmogenic action on guinea-pig ileum and a spasmolytic one on rabbit duodenum. Extracts from *Pithecelobium multiflorum*, *Vitex gardneriana* and *Zizyphus joazeiro* promoted a spasmogenic action on both preparations.

Finally, oxytocic activity upon the rat uterus was shown by extracts from *Annona squamosa*, *Borreria verticilata*, *Byrsonima sericea*, *Cannabis sativa*, *Heliotropium indicum*, *Pithecelobium multiflorum* and *Vitex gardneriana*, whereas inhibition of the oxytocin-induced contractions was shown by extracts from *Coutarea hexandra*, *Simaruba versicolor* and *Tabebuia caraiba*.

DISCUSSION

Much of the literature on the plants examined deals with chemical aspects, few pharmacological results are reported.

Alpinia galanga and *A. officinarum* are official drugs used both as carminative and stimulant. *A. speciosa* is used as an hypotensive but we did not find this action, though there was a stimulant action, on smooth muscle.

Leaves of *Annona muricata* are used as a sedative and a hypnotic. Alkaloids are present in this genus and Burton (1963) studied the biosynthesis of annonaine, an alkaloid of *A. reticulata*.

Byrsonima crassifolia is used in folk medicine against fever, cold and snake-bite. Djerassi, Bowers & others (1956) and Matos, Alencar & others (1968) showed the presence of β-amirin in this species and in *B. sericea*.

Erythrina species have long been known to contain alkaloids with curare-like action. Wasicky & Unti (1952) found the seed extract of *E. crista galli* to possess molluscacidal activity against *Australorbis glabratus* (*sic*). Other species are used in folk medicine as hypnotics, anthelmintics and diuretics.

One of the plants most active on toad isolated heart was *Fagara rhoifolia*. Deulofeu (1946), Moisset de Espanés & Ortega (1946), Moisset de Espanés & Weksler (1946), Calderwood & Fish (1966), von Marquardt (1966) found tertiary and quaternary alkaloids in *Fagara* species. Kuck, Albanico & others (1967) examined the alkaloidal composition of seven *Fagara* species, among them *F. rhoifolia*. The alkaloids, mainly fagarine, reduce myocardial sensitivity and are used in auricular fibrillation, being in some ways superior to quinidine (Hocking, 1955).

The active principle of *Operculina macrocarpa*, the Brazilian jalap, is a purgative glycosidic resin. Some plants of the *Convolvulaceae* family have seeds containing alkaloid with psychotomimetic activity (Claus & Tyler, 1968). The chief active component is ergine, an amide of lysergic acid.

Of the *Cucurbitaceae*, *Luffa operculata* is used as a purgative and an abortifacient. Matos & Gottlieb (1967) identified Isocucurbitacin B, a cytotoxic substance, in the fruits of this plant. Djerassi & others (1956) found gypsogenin in the same plant.

The chemical constituents of *Crataeva roxhburghii* have been shown to be lupeol (Chakravarti, 1959) and an isothiocyanic glycoside, glucopparin (Kjaer & Thomson, 1962). Lupeol is also present in bark of *C. tapia* (Matos & others, 1968).

Cecropia species are cited as folk remedies for the treatment of oedema, asthma, liver diseases and as diuretics and cardioactive agents. According to Feng & others (1962), *C. peltata* presented toxicity to mice and promoted contraction of the guinea-pig ileum, but we didn't verify these effects in *C. carbonaria.*

Plants of the genus *Heliotropium* are rich in alkaloids (Petrova, Deniso & Men'Shikov, 1957; Brutko & Utkin, 1965), mainly heliotropine and casiocarpine. Some of these plants are toxic to mice (Avlyanova, Markmar & Umarov, 1965) but the extract of *H. indicum* was not toxic to mice and fish.

Lantana camara was screened by Hooper & Leonard (1965) whose results were similar to ours.

Matos (1960) found about 3% of total alkaloids in *Peschiera affinis.* Cava, Talapatra & others (1964), identified these as affinine and affinisine.

Pithecelobium saman contains pithecelobine, an alkaloid of unusual structure (Wiesner, 1960) having pharmacological properties (Leonard & Sherrat, 1961, 1967) similar to those of extracts of *P. multiflorum.* This species has a high alkaloid content (Matos & others, 1968).

Both *Solanum torum* and *S. incarnatum* contain steroidal glycosidic alkaloids (Ali, Khan & others, 1967; Fayez & Saleh, 1967).

Doepke (1962) found the alkaloid vitricine in *Vitex trifolia. V. agnus castus* has also been examined and the unsaponifiable part of the seed extract has a progesterone-like effect on rats (Belič, Bergont-Dolar & others, 1958). Ghatuvedi & Sing (1965) found extracts of this plant to have antirheumatic activity superior to salicylate but inferior to cortisone or butazolidine.

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