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Pharmacological Studies of the Bark of *Commiphora africana* (Burseraceae)

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ABSTRACT

Commiphora africana is widely used in traditional medicine as a remedy for some ailments such as stomach pains, dysentery, heartburns and snake-bites. This study was undertaken to evaluate the pharmacological effects of aqueous extract of the stem bark of the plant on isolated rabbit ileum, uterus and heart in order to establish the basis for the use of the plant to treat stomach disorders and some heart related diseases in traditional medicine. Pharmacological screening of the crude aqueous extract of the bark of the plant *Commiphora africana* (Family: Burseraceae) showed a dose dependent relaxation of the isolated rabbit ileum and antagonistic action on the effect of acetylcholine on the same tissue in the same manner as atropine. This has justified the use of the plant for stomach pains and dysentery in traditional medicine. The test on uterus revealed that the aqueous extract lacked agonistic or antagonistic action on the isolated rabbit uterus. However, it showed a dose dependent suppressing action on the rate and the amplitude of the beat of the isolated rabbit heart, a typical **β**-adrenergic antagonistic effect mimicking those potentiated by propranolol. This has also confirmed the basis for the use of the plant to treat heart related problems. Phytochemical analysis revealed the presence of alkaloids, saponins, glycosides and tannins in the plant.

Key words: *Commiphora africana*, Burseraceae, gum-resin, hypertension

INTRODUCTION

Commiphora africana (A. Rich.) Engl. is a species in the family Burseraceae. The plant is called "dashi" in Hausa, "badadi" in Fulani and "kabi" in Kanuri languages of Nigeria (Dalziel, 1937; Keay, 1989). *Commiphora africana* is a bush shrub or small tree mainly found in the savannah woodland and drier parts of tropical Africa. The tree can grow up to 6 m in height but generally the bole is short. The bark is grey or greenish on the bole, reddish on the branches, peeling off in thin papery strips.

The best known products of this family are myrrh, frankincense, American elemi and java almond, which are oleo resins and gums. Myrrh has aromatic acrid and bitter taste. It is made up of volatile oil (2.5-8%), gum (57-61%) and resin (25-35%). It possesses antiseptic and stimulant

properties, hence it is used as an astringent and also as stomachic (Ghani, 1990). Frankincense is mainly used in the preparation of perfumes and incense (Anderson, 1956; Herbert and Ellery, 1948).

Commiphora is a large genus found abundantly in Africa as shrubs or small trees with short trunk and tangled branches. The species of Commiphora yield myrrh, gums and oils resins. The name *Commiphora* is coined from Greek word meaning "gum bearing". This refers to the resin which exudes from the bark of some certain species.

Commiphora africana has been reported in traditional medicine as remedy for some ailments such as stomach pains and dysentery, heart burn and snake-bites. The leaves are pounded with bulrush millet and taken as stomachic. The root is cooked with millet or sorghum to treat heart burns. The stem bark is used to treat diabetic patients, heart burns and as remedy for stomach pains and dysentery. The stem is also used as chewing stick and the wood for making rosary beads (Jinju, 1990). *Commiphora africana* is chiefly noted for its gum resin products some of which are bdellium, galbanum and African myrrh, which are sources of feedstock for making polyester resins, fibres, films, plasters and vanishes (Jessene *et al*., 1987; Rendle, 1952). A chemical study of the bark of the plant was earlier reported from this laboratory (Choudhury *et al*., 2000). This study aimed to evaluate the pharmacological effects of aqueous extract of stem bark of the plant on isolated rabbit ileum.

MATERIALS AND METHOD

The plant materials: The plant materials (stem bark) were collected from a forest near Zaria and authenticated at the Herbarium in the Department of Biological Sciences, Ahmadu Bello University, Zaria, Kaduna State, Nigeria. The plant materials were dried in air under shade for several weeks, crushed and then pounded to powder form. The stem bark powder (100 g) was macerated in distilled water for 24 h. The extract was filtered and lyophilized.

The animals: Three adult female non pregnant rabbits; locally bred (average weight, 1.34±0.05 kg) were used in these tests. Tests on each animal were conducted separately. Each animal was pretreated with 0.1 mg kg^{-1} diethylstilboestrol, 24 h before killing to induce the state of oestrous. 0.1 mg kg^{-1} heparin was injected through the vein in the ear lobe to prevent blood clotting in the heart just before killing. Each animal was killed by a blow on the head and exsanguinated. The abdomen was cut to reveal the uterine horn, the lower intestine and the thoracic region. The following tissues were removed and treated as described below.

Ileum: The ileum part of the small intestine was removed and cut into 3 cm long pieces. Each piece was attached by thread to the lever in the Tyrode solution (Kitchen, 1984), in thermostatically controlled tissue bath (25 mL). The effects of atropine and adrenaline were compared to that of the extract on the tissue.

Uterus: The uterine horns without attached mesentery were mounted in the organ bath (25 mL) containing Dejalon solution (Kitchen, 1984) and well oxygenated at 37°C. The effects of the standard drugs namely: carbochol and acetylcholine were compared with that of the extract on the tissue.

Heart: The heart with trimmed residual fat and adherent tissues was attached to the transducer by means of thread through the aorta and placed in a dish of Ringer-Locke solution

(Kitchen, 1984) at room temperature. The effect of normal saline, acetylcholine, isoprenaline and propranolol were compared with that of the aqueous extract.

RESULTS

The results presented here are the average responses obtained from the tissues of the three rabbits used for the tests.

Rabbit ileum: Acetylcholine (0.4-0.32 g mL^{-1}) produced a concentration-dependent contraction of the isolated rabbit ileum (Table 1). Atropine (0.04-0.32 g mL^{-1}) inhibited the contractions produced by acetylcholine (0.32 g mL^{-1}) (Table 2). The aqueous extract of *Commiphora africana* (CA) relaxed the rabbit ileum and dose dependently (40.0-320.0 mg mL^{-1}) antagonized the effect of acetylcholine (0.32 g mL^{-1}) on the ileum (Table 2).

Rabbit uterus: Carbochol (0.04-0.32 g mL^{-1}) contracted the isolated rabbit uterus (Table 3). Acetylcholine (0.04-0.32 g mL^{-1}) also contracted the isolated rabbit uterus (Table 3). Atropine (0.04-0.32 g mL^{-1}) antagonized the effect of acetylcholine (0.32 g mL^{-1}) on the tissue (Table 3). The aqueous extract of the *Commiphora africana* (40.0-320.0 mg mL^{-1}) did not show any observable response on the uterus. Moreover the aqueous extract of the plant did not change the responses of either acetylcholine or carbochol on the tissue (Table 4).

Table 1: Effect produced by aqueous extract of *C. africana* (CA), acetylcholine (Ach) and atropine (Atr) on the isolated rabbit ileum

Conc. of CA (mg mL^{-1})	Conc. of Ach (g mL^{-1})	Conc. of Atr (g mL^{-1})	Av. resp. of CA (mm)	Av. resp. of Ach (mm)	Av. resp of Atr (mm)	Log-dose of CA	Log-dose of Ach	Log-dose of Atr	% Resp. of CA	% Resp. of Ach	% Resp. of Atr
40	0.04	0.04	75±0.31*	18±0.50*	75±0.28*	1.60	-1.40	-1.40	100	18	100
80	0.08	0.08	70±0.32*	33±0.50*	67±0.30*	1.90	-1.10	-1.10	93	33	89
160	0.16	0.16	57±0.29*	75±0.40*	49±0.40*	2.20	-0.80	-0.80	76	75	65
320	0.32	0.32	15±0.45*	100±0.20*	28±0.40*	2.50	-0.50	-0.50	20	100	37

*p<0.005 (ANOVA, LSD post hoc), Values of responses shown are Mean±SEM (n = 4)

Table 2: Effect of interaction of acetylcholine (0.32 g mL^{-1}) with atropine and acetylcholine (0.32 g mL^{-1}) with aqueous extract of *C. africana* (CA) on isolated rabbit ileum

Conc. of CA (mg mL^{-1})	Conc. of atropine (g mL^{-1})	Average response of CA (mm)	Average response of atropine (mm)	Log-dose of CA	Log-dose of atropine	% Response of CA	% Response of atropine
0	0.00	75±0.4*	75±0.41*	0.00	0.00	100	100
40	0.04	70±0.2*	75±0.32*	1.60	-1.40	93	100
80	0.08	45±3.0*	60±0.29*	1.90	-1.10	60	80
160	0.16	20±0.2*	38±0.45*	2.20	-0.80	27	51
320	0.32	4±0.2*	15±0.23*	2.50	-0.50	5	20

*p<0.005 (ANOVA, LSD post hoc), Values of responses shown are Mean±SEM (n = 4)

Table 3: Effect produced by Aqueous extract of *C. africana* (CA), Acetylcholine (Ach) and carbochol (Carb.) on the isolated rabbit uterus

Conc. of CA (mg mL^{-1})	Conc. of Ach (µ mL^{-1})	Conc. of Carb. (µ mL^{-1})	Av. resp. of CA (mm)	Av. resp. of Ach (mm)	Av. resp of Carb. (mm)	Log-dose of CA	Log-dose of Ach	Log-dose of Carb.	% Resp. of CA	% Resp. of Ach	% Resp. of Carb
40	0.04	0.04	0	32±0.10*	25±0.10*	1.6	-1.40	-1.40	0	44	40
80	0.08	0.08	0	42±0.10*	34±0.10*	1.9	-1.10	-1.10	0	58	54
160	0.16	0.16	0	65±0.40*	35±0.10*	2.2	-0.80	-0.80	0	90	56
320	0.32	0.32	0	72±0.20*	63±0.90*	2.5	-0.50	-0.50	0	100	100

*p<0.005 (ANOVA, LSD post hoc), Values of responses shown are Mean±SEM (n = 5)

Table 4: Effect of interaction of acetylcholine (0.32 g mL^{-1}) with atropine and acetylcholine (0.32 g mL^{-1}) with aq. extract of *C. africana* (CA) on isolated rabbit uterus

Conc. of CA (mg mL^{-1})	Conc. of Atr (g mL^{-1})	Average response of CA (mm)	Average response of Atr (mm)	Log-dose of CA	Log-dose of Atr	% Response of CA	% Response of Atr
0	0	30±0.33*	72±0.20*	0	0	100	100
40	0.04	30±0.33*	70±0.05*	1.6	-1.40	100	97
80	0.08	30±0.33*	60±0.06*	1.9	-1.10	100	83
160	0.16	30±0.33*	40±0.10*	2.2	-0.80	100	56
320	0.32	30±0.33*	15±0.55*	2.5	-0.50	100	21

*p<0.005 (ANOVA, LSD post hoc), Values of responses shown are Mean±SEM (n = 5)

Table 5: Effect produced by aqueous extract of *C. africana* (CA), isoprenaline (Isopr.) and propranolol (Propr.) on the isolated rabbit heart

Conc. of CA (mg mL^{-1})	Conc. of Isopr. (g mL^{-1})	Conc. of Propr. (g mL^{-1})	Av. resp. of CA (mm)	Av. resp of Isopr. (mm)	Av. resp of Propr. (mm)	Log-dose of CA	Log-dose of Isopr.	Log-dose of Propr.	%Resp. of CA	%Resp. of Isopr.	%Resp of Propr.
40	0.04	0.04	45±0.05*	55±0.25*	45±0.61*	1.6	-1.40	-1.40	100	73	100
80	0.08	0.08	40±0.10*	65±0.20*	35±0.55*	1.9	-1.10	-1.10	89	87	77
160	0.16	0.16	25±0.20*	70±0.20*	22±0.50*	2.2	-0.80	-0.80	56	93	49
320	0.32	0.32	20±0.10*	75±0.70*	5±0.25*	2.5	-0.50	-0.50	44	100	11

*p<0.005 (ANOVA, LSD post hoc), Values of responses shown are Mean±SEM (n = 5)

Table 6: Effect of interaction of isoprenaline (0.32 g mL^{-1}) with propranolol and isoprenaline (0.32 g mL^{-1}) with aq. extract of *C. africana* (CA) on isolated rabbit heart

Conc. of CA (mg mL^{-1})	Conc. of. propr. (g mL^{-1})	Average Response (mm) of CA	Average response of Propr. (mm)	Log-dose of CA	Log-dose of Propr.	% Response of CA	% Response of Propr.
0	0	60±0.30*	70±0.50*	0	0	100	100
40	0.04	55±0.24*	65±0.50*	1.6	-1.40	92	93
80	0.08	48±0.31*	45±0.40*	1.9	-1.10	80	75
160	0.16	35±0.32*	42±0.20*	2.2	-0.80	58	70
320	0.32	20±0.21*	25±0.30*	2.5	-0.50	33	42

*p<0.005 (ANOVA, LSD post hoc), Values of responses shown are Mean±SEM (n = 5)

Rabbit heart: Isoprenaline (Isopr., 0.04-0.32 g mL^{-1}) increased the rate of the heart beat. Propranolol (Propr., 0.04-0.32 g mL^{-1}) slowed down the rate of the isolated rabbit heart beat (Table 5). The aqueous extract of *Commiphora africana* (CA, 40.0-320.0 mg mL^{-1}) also slowed down the rate of the heart beat of the rabbit (Table 5). The effect of isoprenaline (0.32 g mL^{-1}) was antagonized by Propranolol (0.04-0.32 g mL^{-1}) and aqueous extract of *Commiphora africana* (40.0-320.0 mg mL^{-1}) (Table 6).

DISCUSSION

Rabbit ileum: The standard drugs used were acetylcholine (Ach), Atropine (Atr) and adrenaline (Adr). Acetylcholine (a quaternary ammonium compound) is an acetyl ester of choline. It serves as a neurotransmitter in a number of organs, including neuro-muscular junctions, post ganglionic fibres of both sympathetic and parasympathetic systems (Elliot *et al*., 1977). The two major actions of acetylcholine on the nerves system are: to stimulate the ganglia, adrenal medulla and skeletal muscle and to stimulate the post ganglionic nerve endings in cardiac muscles, smooth muscles and the glands.

Acetylcholine causes the contraction of smooth muscles (Elliot *et al*., 1977) and in the experiment it produced contraction of the rabbit ileum. The aqueous extract of *C. africana* exhibited a dose dependent relaxation of the ileum. This effect is comparable to those of atropine and adrenaline on the ileum.

The extract of *C. africana* might have been mediating muscarinic inhibition similar to those exhibited by atropine or inhibition caused by adrenaline on adrenergic receptors. The extract of *C. africana* dose dependently inhibited the contractions evolved by acetylcholine; this is similar to the effect shown by atropine, suggesting that, the extract might be mediating its relaxant effect through muscarinic receptors. This effect is beneficial in the management of gastro-intestinal disorders thus justifying the use of the plant in stomach disorders in traditional medicine.

Rabbit uterus: The aqueous extract of *C. africana* was found from this study to have no significant action on the contracting activity of acetylcholine on the isolated rabbit uterus and did not exhibit any agonistic or antagonistic effect of its own on the uterus indicating that it may lack abortifacient activity. In fact, there has been no report of the plant being use for this purpose in traditional medicine.

Rabbit heart: Both sympathetic and parasympathetic systems normally exert a tonic effect on the heart at rest. The main effects that sympathetic activity produces are: increased heart rate i.e., positive chronotropic, effect increased force of contraction i.e., positive inotropic effect, effecting all part of the heart; increased automaticity, facilitation of conduction in the atrioventricular (AV) node and reduced cardiac efficiency i.e., oxygen consumption is increased more than cardiac work. These effects result from activation of β-receptor (Rang and Dale, 2007).

In the heart, each cardiac impulse is preceded by a local depolarization in the region of the sinoatrial (SA) node called pacemaker potential. The most characteristic effect of the catecholamines (i.e., adrenaline, noradrenaline and isoprenaline) is to increase the slope of the pacemaker potential so that the firing threshold is reached faster. The heart beats interval becomes shorter and the heart rate increases. The effect of isoprenaline in increasing the rate of pacemaker activity is most spectacular in isolated heart. It increases the rate strength of contraction of the heart partly by increasing the rate at which the contractile elements are activated in both auricle and ventricle (Schild, 1980).

Drugs which reduce the activity of adrenergic receptors reduce automaticity and improve certain types of heart dysfunction. Two classes of adrenergic blockers are used in this context: β-adrenergic blockers such as propranolol, adrenergic neurone blockers such as bretylium.

Propranolol is a β-adrenoceptor blocking agent. It is a competitive antagonist of isoprenaline with identical side chain which allows it to interact with β-receptors and thereby block the effects of adrenergic stimulation mediated through these receptors. Propranolol is nonselective β-blocker with affinity for β-receptors in the heart and smooth muscle.

It acts by blocking the cardiac chronotropic and inotropic β-receptors resulting in a decrease in the heart rate and myocardial contractility.

From the result shown in Table 5, propranolol produced a dose-dependent relaxation effect on the isolated rabbit heart, while isoprenaline showed a dose-dependent contraction on the isolated rabbit heart (Table 5). The aqueous extract of *C. africana* mimicked the actions of propranolol on the isolated rabbit heart.

The effect of isoprenaline on the isolated heart was blocked in the same manner by both propranolol and the aqueous extract of *C. africana* (Table 6).

From the results, it can be seen that the effect of propranolol on the rate and the amplitude of the heart beat i.e., frequency and force of contraction were comparable to those of the aqueous extract of *C. africana*. Since the rate is the function of pacemaker potential and the amplitude the function of the force and energy process which were potentiated by isoprenaline (a selective β_1-receptor), it could be inferred that, $\beta_1$receptor activity predominates and that β-receptors are involved in this mechanism. This can be supported by the result of propranolol-isoprenaline interactions. By way of extension of the same argument, it can be said that since the aqueous extract of *C. africana* interactions with isoprenaline were almost the same as those of propranolol-isoprenaline, the extract is showing propranolol-like actions. Thus it mediates through β_1-receptors and may be regarded as a competitive nonselective blocking agent of the adrenergic β-receptors, just like propranolol (Black *et al*., 1997; Seriabine and Sweet, 1976).

This action of aqueous extract of *C. africana* justifies its use for the treatment of heart burns and opens a new area of further research on how to use the plant in the management of other cardiac related problems like anti-dysrhythmic actions and hypertension.

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