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Evaluation of the purgative properties of the ethanolic extract of *Khaya senegalensis*

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Abstract

The purgative properties of the ethanolic extract of *Khaya senegalensis* was investigated on isolated rat jejunum and the whole animal. The dose–response effect of the extract and the reference drugs - acetylcholine (ACh) and histamine - on rat jejunum was investigated *in vitro*. The *in vivo* experiment consisted of verifying the increase in contractility of the rat jejunum, and also noting the degree of propulsion caused by charcoal meal which acted as a tracer in the rat intestine. The results showed that the percentage maximum change in amplitude and bath concentration for ACh, histamine and extract exhibited dose-dependent response. Maximum contraction was obtained for histamine, ACh and the extract at $1x10^{-2}$ mol/L, $1x10^{-3}$ mol/L and $1x10^{-2}$ mol/L respectively. The results for mean percentage transit time for charcoal showed that the extract produced a similar effect as the reference drug, sodium sulphate, which is an osmotic purgative. The degree of transition exhibited by the charcoal meal was dose-dependent with 600 mg/kg dose having the highest degree of transition. The experiment showed that the extract *Khaya senegalensis* increased gastrointestinal tract motility by acting via muscarinic and histamine receptors similar to effect produced by reference drugs ACh, histamine and sodium sulphate. The extract therefore could be said to exhibit purgative properties and might be of use in management of difficulties associated with defaecation or for constipation.

Keywords: Purgative; Constipation; *Khaya senegalensis*

Introduction

The plant *Khaya senegalensis* Juss (Meliaceae) was reputed as medicinal. It is a dry zone mahogany widely distributed in the Savannah region; recognized by round evergreen crown of dark shining foliage, pinnate leaves and characteristic round capsule (*Sofowora*, 1993). It is often planted by road side for shade. The bark is very bitter and has considerable reputation among the people as a fever remedy, taken as fresh bark mixed with salt and taken in small quantity every second day. It is very much rarely used as a bitter tonic. In French West African Colonies it is used for treating syphilis and as a purgative. The bark is also used in native veterinary practice as a dressing for ulcers on the back of camels (Dalziel and Hutchinson, 1958).

Purgatives, are medicines that promote defaecation largely by reducing the viscosity of the content of lower colon. Purgatives are

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classified into bulk, osmotic or saline faecal softeners and stimulants (Lawrence and Bunnet, 1996). *Khaya senegalensis* is said to belong to the class of herbs being used as purgative.

Experimental

Plant collection, identification and extraction. The plant stem bark was obtained from a local herb seller and the specimen identified at the Federal School of Forestry, Jos by a plant taxonomist, Mr. Okonkwo. The stem bark was dried in the bark was pulverized to fine powder with the aid of mortar and pestle. 50 g was extracted for 48 hours in Soxhlet extractor, using 350 mL of 99% ethanol at a temperature of 78°C. The ethanolic extract was evaporated in a thermo-regulated organ bath at 70°C until a crude extract of *Khaya senegalensis* was left. Which was hermetically stored in a refrigerator until required for use.

Experimental animals. The rats used for this work were obtained from the animal house University of Jos, and were starved for 24 hours prior to use. Two sets of rats of either sex were used, some for *in vitro* experiment while others were use for the *in vivo* experiment. The rats were killed humanely by a sharp blow to the neck region with the edge of an outstretched palm, after which they were exsanguinated and their abdomen cut open. Sections of the small intestine were removed. A suitable length of the jejunum was cut (2-3cm) and the mesenteric attachment detached from it. The lumen of the tissue was flushed using tyrode solution. With the aid of a 5mL pipette and quickly with a thread and needle the two ends of the jejunum were tied with one long and the other short thread. The shorter end of the thread was tied to the hook of the aerator suspended in the 50mL organ bath and the other end, which has the longer thread, was tied on the lever carrying the writing pen. The tissue was then incubated for 20 minutes during which time the solution was aerated and maintained at a temperature of 37°C with a pH of 7.4 for equilibration. After the equilibration and normal contractility has been established, the tissue was challenged with the prepared concentrations of the extract and the reference drugs (ACh and histamine). 1mL of different concentrations of the drugs were used and responses recorded was on the kymograph drum.

After injecting particular concentration and observing the effect, the drug was washed out and a fresh tyrode solution was poured into the organ bath. Time was allowed for equilibration of the tissue for normal contractility to be established.

Administration of charcoal meal. The method used was as modified by Williamson *et al* (1996). Twenty five rats divided into five (5) groups of 5 rats each and were administered with the substances indicated.

Group I - 1mL of normal saline and 1mL of charcoal meal orally.

Group II - 200mg/kg of extract and 1mL of charcoal meal orally.

Group III - 400mg/kg of extract and 1mL of charcoal meal orally.

Group IV - 600mg/kg of extract and 1mL of charcoal meal orally.

Group V - 1mL/kg of 1 M Na_2SO_4 solution.

The charcoal meal served as a tracer for motility. Thirty minutes after administration, the rats were sacrificed and the intestine spread out, the length from the duodenum to the ileo-caecal junction was measured and recorded.

Results and discussion

The results from the *in vitro* experiment on rat jejunum showed that there was a contractile response to the reference drugs ACh and histamine. ACh gave a dose dependent response on the rat jejunum, similar effect was observed with histamine and the results showed that the effect was dose dependent as in Tables 1 and 2. The

extract showed similar effect as the reference drugs and its response was also dose dependent as in Table 3.

Table 1: Effects of graded doses of histamine on rat jejunum.

Drug concentration (mol/L)	Volume of histamine administered (mL)	Final bath concentration (mol/L)	Log of final bath concentration	Normal amplitude of contraction (cm)	Amplitude due to histamine (cm)	Percentage of maximum change in amplitude
$1x10^{-7}$	1.0	$2x10^{-5}$	-8.6990	1.0	1.7	58
$1x10^{-6}$	1.0	$2x10^{-4}$	-7.6990	1.0	1.5	42
$1x10^{-5}$	1.0	$2x10^{-5}$	-6.6990	1.0	1.9	75
$1x10^{-4}$	1.0	$2x10^{-6}$	-5.6990	1.0	2.0	83
$1x10^{-3}$	1.0	$2x10^{-5}$	-4.6990	1.0	1.8	67
$1x10^{-2}$	1.0	$2x10^{-4}$	-3.6990	1.0	2.2	100

Table 2: Effects of graded doses of acetylcholine on rat jejunum

Drug concentration (mol/L)	Volume of ACh administered (mL)	Final bath concentration (mol/L)	Log of final bath concentration	Normal amplitude of concentration (cm)	Amplitude due to ACh (cm)	Percentage of maximum change in amplitude
$1x10^{-7}$	1.0	$2x10^{-5}$	-8.6990	2.0	3.3	33
$1x10^{-6}$	1.0	$2x10^{-4}$	-7.6990	2.5	4.3	43
$1x10^{-5}$	1.0	$2x10^{-5}$	-6.6990	3.0	5.0	40
$1x10^{-4}$	1.0	$2x10^{-6}$	-5.6990	1.8	5.0	69
$1x10^{-3}$	1.0	$2x10^{-5}$	-4.6990	0.5	2.0	100
$1x10^{-2}$	1.0	$2x10^{-4}$	-3.6990	1.0	1.8	45

Table 3: Effects of graded doses of extract on rat jejunum

Drug concentration (mol/L)	Volume of extract used (mL)	Final bath concentration (mol/L)	Log of final bath concentration	Normal amplitude of contraction (cm)	Amplitude due to extract (cm)	Percentage of maximum change in amplitude
$1x10^{-7}$	1.0	$2x10^{-9}$	-8.6990	6.9	0.52	35
$1x10^{-6}$	1.0	$2x10^{-8}$	-7.6990	1.0	1.1	55
$1x10^{-5}$	1.0	$2x10^{-7}$	-6.6990	1.0	1.5	75
$1x10^{-4}$	1.0	$2x10^{-6}$	-5.6990	0.8	2.6	80
$1x10^{-3}$	1.0	$2x10^{-5}$	-4.6990	0.6	2.0	90
$1x10^{-2}$	1.0	$2x10^{-4}$	-3.6990	0.5	1.0	100

Table 4: Charcoal transit time - Group I

Weight of rats (g)	Volume of extract administered (mL)	Volume of charcoal meal administered (mL)	Length of intestine (mm)	Distance travelled by the charcoal meal (cm)	Velocity of Charcoal meal (cm/min)	Mean percentage distance traveled by the charcoal meal
90	-	1.0	72.0	50.0	1.7	69.4± 0.6
120	-	1.0	74.0	50.0	1.7	67.6± 1.0
100	-	1.0	84.0	71.0	2.3	81.6± 2.1
103	-	1.0	83.0	50.5	1.6	70.5± 4.0
110	-	1.0	85.0	61.0	2.0	72.1± 0.5

Table 5: Charcoal transit time - Group II

Weight of rats (g)	Volume of extract administered (mL)	Volume of charcoal meal administered (mL)	Length of intestine (mm)	Distance travelled by the charcoal meal (cm)	Velocity of Charcoal meal (cm/min)	Mean percentage distance traveled by the charcoal meal
115	0.23	1.0	98.0	76.0	2.5	77.6±0.7
125	0.25	1.0	109.6	68.0	2.3	62.4±2.6
134	0.27	1.0	135.0	74.0	2.5	84.8±0.4
130	0.26	1.0	132.0	105.4	3.5	80.1±1.0
138	0.28	1.0	136.0	102.0	3.4	75.1±0.2

Table 6: Charcoal transit time - Group III

Weight of rats (g)	Volume of extract administered (mL)	Volume of charcoal meal administered (mL)	Length of intestine (mm)	Distance travelled by the charcoal meal (cm)	Velocity of charcoal meal (cm/min)	Mean percentage distance traveled by the charcoal meal
125	0.56	1.0	94.0	96.0	2.5	80.9± 0.7
105	0.40	1.0	93.0	68.0	2.3	73.1± 2.5
123	0.50	1.0	74.0	74.0	2.5	100.0± 3.7
140	0.56	1.0	139.5	117.2	3.9	34.3± 0.1
139	0.66	1.0	137.0	110.3	3.7	80.6 ± 0.8

Table 7: Charcoal transit time - Group IV

Weight of rats (g)	Volume of extract administered (mL)	Volume of charcoal meal administered (mL)	Length of intestine (mm)	Distance travelled by the charcoal meal (cm)	Velocity of charcoal meal (cm/min)	Mean percentage distance traveled by the charcoal meal
110	0.75	1.0	84.0	74.0	2.5	88.1± 1.1
115	0.84	1.0	85.0	77.0	2.6	90.6±0.5
110	0.63	1.0	80.0	72.0	2.7	94.1±0.2
120	0.90	1.0	140.0	135.0	4.5	95.4± 0.2
125	0.84	1.0	45.0	140.9	4.7	97.2± 0.1

Table 8: Charcoal transit time - Group V

Weight of rats (g)	Volume of extract administered (mL)	Volume of charcoal meal administered (mL)	Length of intestine (mm)	Distance travelled by the charcoal meal (cm)	Velocity of Charcoal meal (cm/min)	Mean percentage distance traveled by the charcoal meal
118	0.125	1.0	84.0	62.0	2.1	73.8± 1.9
105	0.140	1.0	97.3	75.0	2.5	75.9± 1.5
110	0.102	1.0	72.5	70.0	2.3	97.2± 3.4
115	0.130	1.0	128.0	102.4	3.4	80.0± 0.5
120	0.135	1.0	130.0	109.2	3.6	84.0± 0.4

Results from *in vivo* experiment for Charcoal transit time showed that Thirty minutes after administration of reference drug (Na_2SO_4), there was an increase in propulsion with the Charcoal meal when compared with the control group indicating an increase in motility of the intestine. The extract also caused an increase in propulsion with the charcoal meal when compared to the control group, indicating an increase in motility of the rat jejunum. The degree of motility was dose dependent as shown in Tables 4 to 8.

From the results obtained from the *in vitro* experiments using the rat jejunum, it was found that the extract caused an increase in amplitude similar to that produced by acetylcholine which is a muscarinic receptor agonist whose activity increased contraction of the rat Jejunum via muscarinic receptors (Lawrence and Bunnet, 1996, Ganong, 1998).

The results of percentage maximum change in amplitude and bath concentration in tables 1,2 and 3 showed that acetyl choline, histamine and the extract exhibited a dose dependent response. The maximum contraction was obtained for histamine at a response of $1x10^{-2}$ mol/L, for acetyl choline at $1x10^{-3}$ mol/L, while for the extract, the maximum response was obtained at $1x10^{-2}$ mol/L.

The results for mean percentage transit time for charcoal meal showed that the extract exerted similar effect with the reference drug sodium sulphate which is an osmotic purgative (Lawrence and Bunnet, 1996). The results also showed that the degree of transition exhibited by the charcoal meal was dose dependent with the 600 mg/kg dose having the highest degree of transition.

The contractile effect exhibited by the rat jejunum suggests that the extract could be used in constipation crisis which is characterized by difficulty in defaecation (Sofowora 1993, Dalziel and Hutchinson, 1958). The overall evaluation of the ethanolic extract of *Khaya senegalensis* compared with the reference drug Na_2SO_4 in the overall transit time experiment showed that at 400 mg/kg and 600 mg/kg the contractions obtained were higher and was dose dependent.

Na_2SO_4 as an osmotic purgative exerts its effect by preventing water absorption by gastrointestinal tract through its osmotic property (Lawrence and Bunnet, 1996). These osmotic properties cause water retention in the lumen of the GIT thereby increasing the bulk of the intestinal content which brings about a stretch on the walls of the intestine, hence the reflex stimulation cause normal contractility and defaecation. Acetylcholine and histamine act *via* muscarinic and histamine receptors respectively, they bind and stimulate these receptors causing the smooth muscles of the gastrointestinal tract to contract (Lawrence and Bunnet 1996, Ganong, 1998). From the results obtained it can be deduced that the mechanism of action of the extract might be by binding to muscarinic and histamine receptors and causing the smooth muscle of the gastrointestinal tract to contract. More work need to be done to elucidate this mechanism of action of the extract and other pharmacological properties of the extract.

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