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# Screening for the Ethno-Putative Therapuetic Activity of Ox Bile

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**Abstract:** Ox bile has ethno-pharmacological uses in Sudan. To verify this putative therapeutic value, it was screened for activity using standard pharmacological methods. Three isolated tissues were subjected to fresh Ox bile; the rabbit intestine, the rat aorta and uterus. About 0.5 μL $mL^{-1}$ of bile relaxed rabbit intestinal contractions by 64.9%. And 1.0 μL $mL^{-1}$ of bile relaxed rabbit intestinal contractions by 78.4%, 2.0 μL $mL^{-1}$ of bile relaxed rabbit intestinal contractions by 100%, 0.5 μL $mL^{-1}$ of bile relaxed rabbit intestinal contractions that had been treated with 1.25 μg $mL^{-1}$ of phentolamine plus 1.25 μg $mL^{-1}$ of propranolol by 65.9%. About 1.0 μL $mL^{-1}$ of bile relaxed rabbit intestinal contractions that had been treated with 2.50 μg $mL^{-1}$ of phentolamine plus 2.50 μg $mL^{-1}$ of propranolol by 80%. About 1.0 μL $mL^{-1}$ of bile abolished aortic strip contraction and tone to 1.0 μg $mL^{-1}$ noradrenaline, 0.5 μL $mL^{-1}$ abolished aortic strip contraction and tone to 1.0 μg $mL^{-1}$ noradrenaline. About 0.25 μL $mL^{-1}$ abolished aortic strip contraction to 1.0 μg $mL^{-1}$ noradrenaline, residual tones were recorded every 3~4 sec. About 2, 1 and 0.5 μL $mL^{-1}$ of bile abolished aortic strip contractions and tone to 0.12 μg $mL^{-1}$ noradrenaline. About 2, 1 and 0.5 μL $mL^{-1}$ of bile abolished aortic strip contractions and tone to 0.16 μg $mL^{-1}$ noradrenaline. About 1 μL $mL^{-1}$ of bile abolished aortic strip contractions to 0.2 μg $mL^{-1}$ noradrenaline and 0.2 μg $mL^{-1}$ adrenaline, residual tone persisted. About 2 μL $mL^{-1}$ of bile relaxed uterine contractions by 52.6%. About 4 μL $mL^{-1}$ relaxed uterine contractions by 42%. And 6 μL $mL^{-1}$ relaxed uterine contractions by 46.4%. About 8 μL $mL^{-1}$ relaxed uterine contractions by 48.95%. And 10 μL $mL^{-1}$ relaxed uterine contractions by 51.5%. About 12 μL $mL^{-1}$ relaxed uterine contractions by 72.2%. About 16 μL $mL^{-1}$ relaxed uterine contractions by 62.5%. About 20 μL $mL^{-1}$ relaxed uterine contractions by 62.5%. About 40 μL $mL^{-1}$ relaxed uterine contractions by 75%. Statistical verification of uterine relaxations to bile determined significant individual tissue variations.

**Key words:** Ox bile, spasmolytic, vasodilator, utero-spasmolytic, tissue variations, uterine

## INTRODUCTION

This research is an extension of a previous research on Ox bile (Abdelhalim, 2004) that had focused on the mechanisms and factors contributing to a potential toxicity of Ox bile traditionally believed to ensue under certain circumstances.

Bile has established itself in the local ethno-pharmacology particularly in Darfur states as a remedy for a diversity of conditions that extend from indigestion to toothache, application to open wounds, hypertension, infertility or an inducer of childbirth.

Being a nutraceutical (feedstuff that have therapeutic value in addition to its known nutritional value), it is commonly consumed if not for a particular therapeutic purpose then as an appetizer or merely a condiment.

Rational use of bile developed as an extension of its known physiologic role, its utilization as a cholagogue (stimulation of bile secretion), a stimulant of digestion and absorption and in the prevention and mobilization of gallstones has been stated by Bockus (1953), Podda *et al.* (1982) and Hofmann (1999). Rational uses of bile acids have utilized their selective antimicrobial actions by their incorporation in certain selective media such as McConkey (Collee *et al.*, 1996). The fact that most modern investigations focused on bile acids rather than bile, despite reports of the different actions of the two substances (Rampone, 1972a) has provoked the present investigation to verify and discern its pharmacological actions by experimental methods with a view to identify scientific evidence that support or contradict putative therapeutic uses.

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## MATERIALS AND METHODS

**Drugs:** The drugs that were used with the doses mentioned in the following text and figures refer to the following compounds:

- Noradrenaline; L-Noradrenaline 98% produced by Alfa Aesar', Lancaster, England
- Adenaline; L-Adrenaline 98% produced by Alfa Aesar', Lancaster, England
- Phentolamine; Phentolamine hydrochloride produced by Pharma Drug Production GmbH, Hambourg, Allemange
- Propranolol; Propranolol hydrochloride, Fluka Chemie GmbH, Sigma-Aldrich, Production of USA
- Ethinyl Oestradiol, Pfizer Laboratories, Germany

**Physiological salts solutions:** Physiological salts solutions were made by dissolving in distilled water of salts of the Analytical Research grade (ANALAR) brand produced by Hopkin and Williams Ltd., England.

- Krebs solution; its composition was as described by Krebs and Henseleit (1932). The solution contained (g $L^{-1}$): NaCl 6.9, KCl 0.35, $CaCL_2$ 0.28, $KH_2PO_4$ 0.14, $MgSO_4$ 0.11, $NaHCO_3$ 2.1 and dextrose 2
- De Jalon's solution; it contained (g $L^{-1}$): NaCl 9, KCl 0.42, $CaCL_2$ 0.04, $NaHCO_3$ 0.5 and glucose 0.5
- Tyrode's solution contained (g $L^{-1}$): NaCl 8, KCl 0.2, $CaCL_2$ 0.26, $NaH_2PO_4$. $2H_2O$ 0.065, $MgSO_4$ .$7H_2O$ 0.26, $NaHCO_3$ 1.0 and glucose 1

The preparation of De Jalon and Tyrode solution followed the description recommended by University of Edinburgh, Department of Pharmacology (1970).

**Instruments:**

- Student oschillograph produced by Harvard Apparatus Ltd., Edenbridge, Kent
- Grant Y14 Waterbath produced by Grant Instruments, Cambridge, England
- Electronic balance type AY220 produced by Shimadzu, Japan

**Isolated tissue preparations**

**Rabbit intestine:** These preparations were made in accordance with the method described by Thompson (1990). Rabbits weighing 2~3 kg that had been fasted for 24 h from food but not water were exsanguinated using a scalpel and blade, the contents of the gut were exposed by a midline incision on the abdomen, a substantial length of ileum was carefully removed using scissors into a petri dish that contained Tyrode's solution with air being bubbled into it, residual ingesta contents were carefully washed out of these segments of ilea by a 30 mL syringe filled with Tyrode's solution omental segments were trimmed off and ilea cut several pieces 2-3 cm long. These were set up for testing antispasmodic activity according to the method adapted by Boura (1954), one of a 2~3 cm ilea strip was tied with a piece of thread to a fixed glass rod into the other end of the tissue an S-shaped hook to which an ample length of thread had been tied was inserted.

The glass rod and ileal strip were then placed into a 50 mL Magnus tissue path containing Tyrode's solution, warmed up to 37°C and constantly aerated. The loose end of the thread was then attached into a force displacement clonic transducer in an adjustment set to exert only a 0.5 g tension on the tissue, the transducer had been connected to a recording oschillograph. The muscle was allowed to equilibrate for up to 30 min, spontaneous rhythmicity instituted and recorded.

**Rat aorta:** The aortic strip preparations were made following the method described by Thompson (1990). Young white albino rats weighing >150 g were each stunned by a blow on the head and rapidly bled by exsanguination. The visceral contents and abdominal aorta were exposed by midline incisions using scalpel and blade. Aorta were dissected from adhering fat and connective tissue, cut and removed into petri dishes that contained constantly aerated Krebs solution at room temperature.

A thin glass rod was inserted into each aorta and the vessel cut into helical spiral strips as had been described by Forchgott and Bhadrakom (1953), each helical strip was furthermore cut into pieces 7-10 mm long and 0.8 mm wide. These were mounted into 50 mL tissue baths containing constantly aerated Krebs solution, the lower ends were attached to a fixed lever in the bath whereas the upper ends were attached by means of size 000 threads to force displacement transducers adjustments that generated 0.5 g passive tensions.

**Rat uterus:** Female white albino rats, 8 weeks of age weighing 120~150 g were synchronized into oesterus by administering oral ethinyl oestradiol (250 ug $kg^{-1}$) 48 h beforehand (Thompson, 2001). Uterus tissues were prepared according to the method endorsed by University of Edinburgh, Department of Pharmacology (1970).

Rats were exsanguinated, abdomens opened, uterine horns dissected out and transferred to petri dishes that contained De Jalon's solution. The two horns of each uterus were separated and freed from fat and each was cut longitudinally into a sheet of muscles that was furthermore longitudinally halved.

A thread was attached of each end of each piece and the preparation was usually mounted in a constantly aerated De Jalon's solution. One thread was attached to

a fixed pin and the other to a lever fit into a force displacement transducer connected to a recording oschillograph, the load on the lever was usually adjusted to about 0.5 g and the temperature to 32°C, regular responses were usually taken after 15~30 min settling down allowance.

**Bile collection:** Fresh Ox bile samples were collected (twice a week) during the postmortem inspection at Sabaloka abattoir, Omdurman, Sudan; 3 mL of bile were taken using sterile syringes from sound gallbladders into sterile Bijou bottles, transported in ice to the laboratory.

**Method of testing drugs on isolated preparations:** The procedures practiced were similar to those described by Tigani (1969). Stock solutions of drugs were made with distilled water and kept in the refrigerator at 5°C for not >1 week. The drugs were diluted to the required concentrations with 0.9% w/v NaCl just before use and used during the same day. Drugs were added to the organ bath with disposable syringes in volumes not exceeding 1% of that of the organ bath. Agonists, particularly adrenaline and noradrenaline on aorta were left in contact with isolated preparations for specified periods of time and the solution in the bath changed twice after each test, the test usually being repeated every 5-10 min. When the responses to agonists became steady, the test Ox bile was added to the bathing solution and its concentration maintained throughout the period of thetest. Whenever possible antagonism was measured in terms of the dose ratio which is the ratio of equi-active concentrations of agonists in the presence and absence of the antagonist. Autonomic receptor blockers notably so phenotolamine and propranolol that had been added to the organ bath in specified concentrations were left in contact with the tissues for specified periods of time, thereafter the test Ox bile was usually adjunctively added to that same solution in the organ bath.

**Statistical analysis:** Conducted using the SPSS computerized program.

## RESULTS AND DISCUSSION

**The pharmacology of Ox bile on the rabbit isolated intestinal preparation:** These tissues had exhibited pronounced spontaneous rhythmic contractions not interrupted by relaxations as long as tissues remained vivid. Tissue responses to varying dose concentrations of Ox bile in a decreasing schedule are shown in Fig. 1. About 2, 1 and 0.5 μL $mL^{-1}$ of Ox bile promptly suppressed the contracting tissues 100, 78.4±5.4 and 64.9±8.1%, respectively, n = 6 observation. Suppressions were reversible; tissues resumed equal movements upon washing. Rabbit isolated intestinal preparations primed with 1.25, 2.5 and 5 μg $mL^{-1}$ phentolamine for 5~20 min exhibited no change in their pattern of innate contractions, administration of (1 μL $mL^{-1}$) of the test Ox bile reduced these contractions by 59.55±7.15, 69±11.9 and 64.25±7.15%, respectively, n = 6 observations, depressions were fully reversible (Fig. 2). Preparations primed with 5~20 min exposures to propranolol 0.6, 1.25, 2.5 and 5 μL $mL^{-1}$ were depressed by 1 μL $mL^{-1}$ doses of Ox bile 50.1±18.7, 59.4±9.4, 65.7±15.6 and 45.5±9%, respectively, n = 6 observations depressions were readily reversible (Fig. 3).

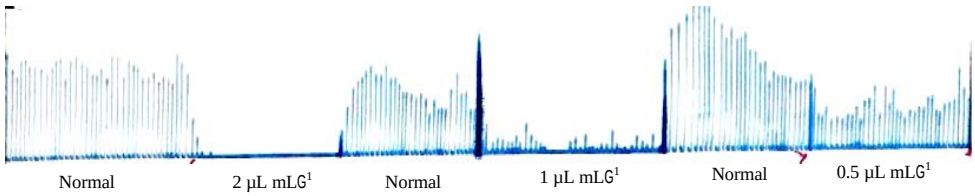


Fig. 1: Rabbit, isolated intestinal tissue preparation, prompt reversible inhibitory effects on spontaneous contractions by 2, 1 and 0.5 μL $m^{-1}$ of Ox bile; 2.5 mm = 1 sec

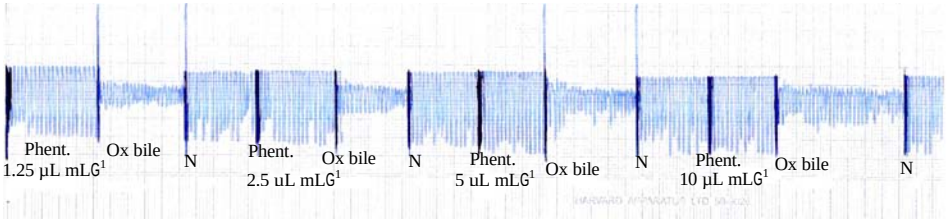


Fig. 2: Rabbit, isolated intestinal tissue preparation showing prompt reversible relaxations of spontaneous contraction by 1 μL $mL^{-1}$ of bile of Ox although the indigenous inhibitory α-receptors have been blocked by 5-20 min exposures to 1.25, 2.5, 5 and 10 μL $mL^{-1}$ phentolamine; 2.5 mm = 1 sec

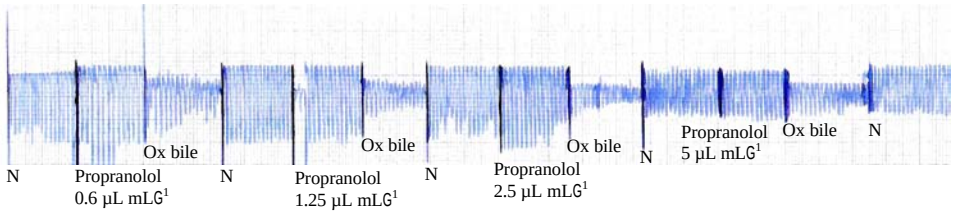


Fig. 3: Rabbit, isolated intestinal tissue preparation showing abrupt reversible relaxations of spontaneous contraction by 1 µL mL$^{-1}$ of bile of Ox wherein the natural inhibitory α-receptors of the tissue had been blocked by 5-20 min exposures to 0.6, 1.25, 2.5 and 5 µL mL$^{-1}$ propranolol; 2.5 mm = 1 sec

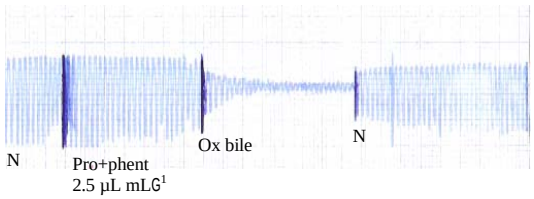


Fig. 4: Rabbit, isolated intestinal tissue preparation, exhibiting abrupt reversible relaxations of rhythmic spontaneous contractions to 1 µL mL$^{-1}$ of Ox bile wherein both inhibitory α and β receptors have been blocked by 5-20 min exposures to adjunctive phentolamine and propranolol (2.5 µg mL$^{-1}$ each); 2.5 mm = 1 sec

Those intestinal preparations exposed to 5~20 min contemporary adrenergic blocker treatments with phentolamine and propranolol at equal adjunctive dose of 1.25 and 1.25, 2.5 and 2.5 or 5 and 5 µg mL$^{-1}$ showed no significant changes in their spontaneous contractions, prompt inhibitions were generated by 1 µL mL$^{-1}$ of Ox bile 65.9±6.8, 80.6±8.3 or 77.8±5.6%, respectively, n = 6 observations, no untoward tissue damages were observed, tissues resumed full rhythm upon washing (Fig. 4) shows such effects.

**Statistical verification of inhibition on intestinal tissue:** When the activities of Ox bile on intestinal tissues were compared with those inhibitions on intestinal tissue under blockade with phentolamine and propranolol no significant differences were obtained (significance $p<0.05$) (Fig. 5a-c).

**The pharmacology of Ox bile on the rat isolated aorta:** The responses of the rabbit isolated aorta to 5~30 min exposures to 0.1, 0.12, 0.16 and 0.2 µg mL$^{-1}$) of noradrenaline had followed a dose related fashion generating tissue tones that tended to increase in frequency, interrupted every 2 sec by small contractions that increased in magnitude and less so frequency following dose increments. In aortic strip preparations responding to 20 min exposure to 0.1 µg mL$^{-1}$ noradrenaline, 1 µL mL$^{-1}$ of Ox bile abolished both contractions and tones 100% (0.5 and 0.25 µL mL$^{-1}$) nevertheless abolished both however, extremely small twitches were recorded every 3~4 sec (Fig. 6), it is worth noting that the suppressant activities of bile were prompt and that the tissues failed to resume neither contractions nor tones after several washes. The contractions of the rabbit isolated aortic preparations to exposures to 0.2 µg mL$^{-1}$ noradrenaline were sustained short contractions interrupted every 1~2 sec by relatively higher contractions (2 µL mL$^{-1}$) of Ox bile brought about prompt almost absolute, cessations of these responses 1 as well as 0.5 µL mL$^{-1}$ of Ox bile generated prompt, likewise cessations of aortic contractions to this concentration of noradrenaline. However, following washing tissues were not as quiescent as previously observed, contractility was reinstituted (Fig. 7) indicating residual catecholamine activities in the vicinity and once more confirming the characteristic reversible nature of these inhibitory actions of Ox bile. Rat isolated aorta preparations responses to 30 min exposures to adjunctive adrenaline and noradrenaline (0.2 µg mL$^{-1}$ each) ensued sustained vigorous contractions contributing the usual previously observed tone (1 µL mL$^{-1}$) Ox bile abolished these contractions whereas residual tone persisted (Fig. 7).

**Pharmacological activities of Ox bile on uterine contractions:** The inhibitory activities of Ox bile on rat isolated uterine tissues contracting to 0.01 mg kg$^{-1}$ oral ethinyl oestradiol are shown in Fig. 8 and 9. About 2 µL mL$^{-1}$ of Ox bile abruptly inhibited uterine contractions (60.3±4 and 52.6%), inhibition was fully reversible by washing, n = 3 observations. About 4 µL mL$^{-1}$ of Ox bile immediately suppressed uterine contractions by 55.6±5.6, 42, 65.3±7, 46.5±3.6 and 48.1±1.9%, suppressions were readily reversible by washing, n = 7 observations. About 6 µL mL$^{-1}$ of Ox bile promptly depressed uterine contractions by 61.5, 46.4±1.4, 68.75, 55.85 and 57.8%, depression were abolished by washing, n = 7 observations.

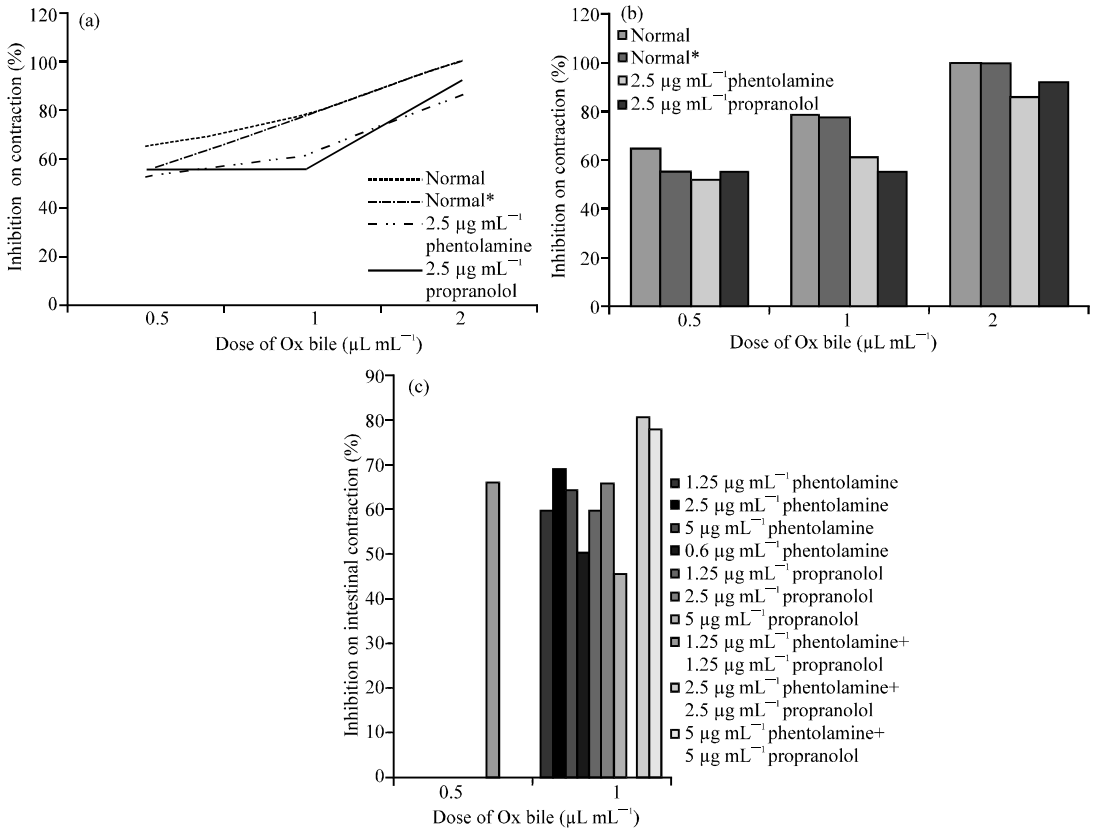


Fig. 5: Inhibition on different isolated intestinal preparations by different doses of Ox bile after blocking; a, b) by phentolamine, propranolol or both; c) by phentolamine, propranolol and both

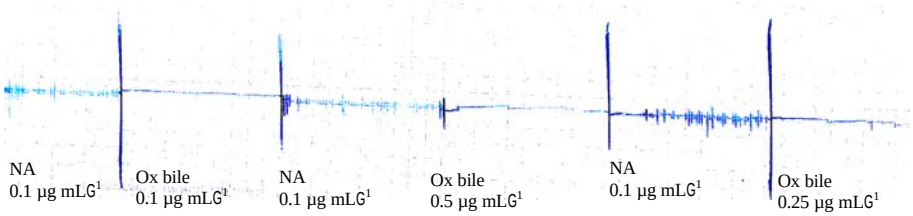


Fig. 6: Rat, isolated aorta, contracting to 20 min exposure to 0.1 µg mL$^{-1}$ noradrenaline and showing prompt relaxations to 1, 0.5 and 0.25 µL mL$^{-1}$ of Ox bile, 3-4 sec interval twitches are apparent; 2.5 mm = 1 sec

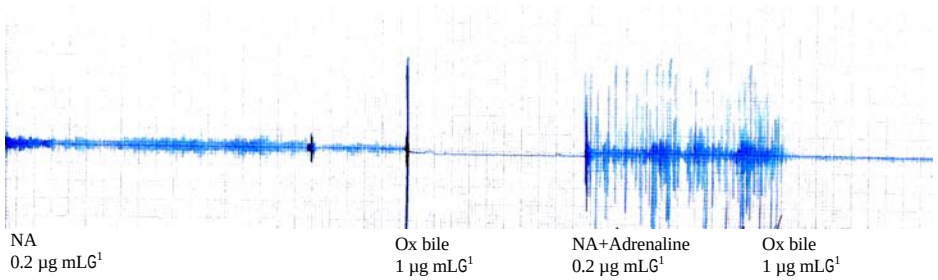


Fig. 7: Rat, isolated aorta, vigorously contracting to 30 min noradrenaline and adrenaline adjunctively (0.2 µg mL$^{-1}$ each) displaying cessation of contractions by 1 µL mL$^{-1}$ of Ox bile, residual tone persists; 2.5 mm = 1 sec

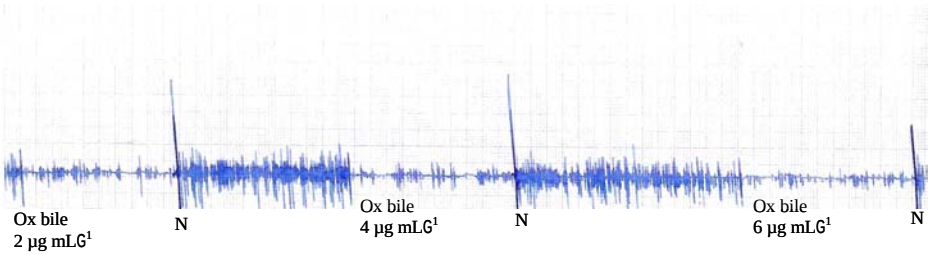


Fig. 8: Rat, ethinyl oestradiol. Inhibitory effects on uterine contractions by 2, 4 and 6 µL $mL^{-1}$ of Ox bile, the instantaneous onset and full recovery after each washing; 2.5 mm = 1 sec

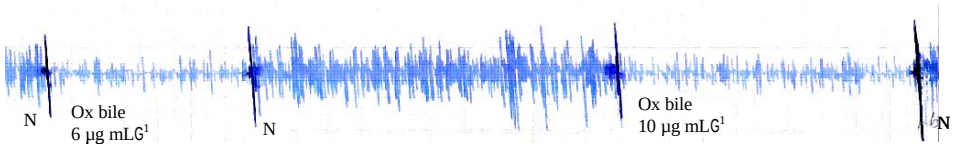


Fig. 9: Rat, ethinyl oestradiol; instantaneous depression of vigorous uterine contractions by 6 and 10 µL $mL^{-1}$ of Ox bile; the tissue resumes full contractility upon removal of bile by washing; 2.5 mm = 1 sec

About 8 µL $mL^{-1}$ of Ox bile immediately inhibited uterine contractions by 48.95, 72.2, 65.2±1.6 and 67.5±1.3%, inhibition was immediately removed by washing, n = 6 observations. About 10 µL $mL^{-1}$ of Ox bile abolished uterine contractions by 51.5±8.6, 72.2, 65.35 and 63.1%, inhibition immediately ensued and so were recoveries upon washing, n = 5 observations. About 12 µL $mL^{-1}$ of Ox bile inhibited uterine contractions abruptly by 50.75, 72.2, 65.5±5 and 58.7±1.3%. Inhibition were readily reversible by washing, n = 7 observations. About 16 µL $mL^{-1}$ of Ox bile promptly abolished uterine contractions by 50 and 62.5%, tissue resumed full contractility after washing, n = 5 observations.

About 20 and 40 µL $mL^{-1}$ of Ox bile immediately depressed uterine contractions by 65.2 and 75%, respectively, inhibition was readily reversible by washing, n = 3 observations.

**Individual uterine response variation to inhibition by Ox bile:** From Fig. 10a and b, it was discerned that individual uterine tissues exhibited commensurate inhibitions to the varying Ox bile dosing, statistical analysis determined no significant differences in response of the same uterine tissue to exponentially folding Ox bile dose regime. However, when the responses of individual uterine tissues to these specific does were compared, statistically significant differences were obtained (significance $p<0.05$).

The present investigation sheds light on the pharmacodynamic actions of bile on the innate contractions of the rabbit isolated intestine, contractions of the rat isolated aorta to catecholamines and rat uterus made contractile by beforehand bringing the animals into

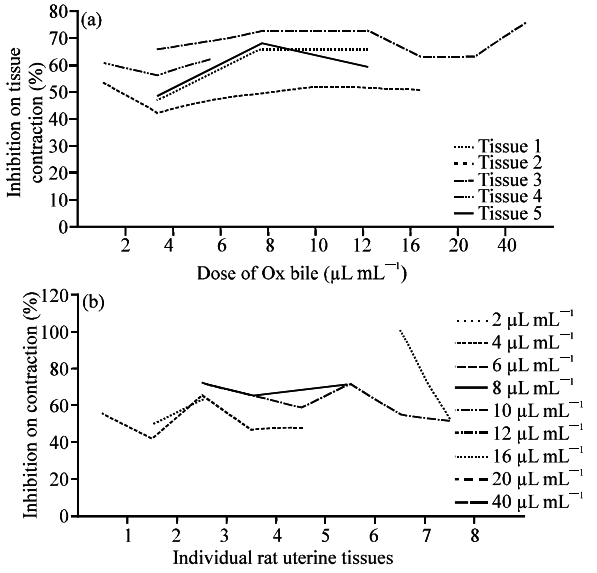


Fig. 10: a, b) Individual uterine tissue reaction to different doses of Ox bile

estrus. The prevalent sole relaxant action on this diversity of contractions suggests the high likelihood that bile directly acts on the smooth muscle of these tissues. The prompt, readily demonstrable, dose related manner of these actions suggest the non failing efficacy and high potency of this substance, this is consistent with the observations by Rampone (1972b) who demonstrated marked reduction in cholesterol or fatty acids uptake by tissue after the addition of only 0.25 mL of whole bile to the usual 25 mL incubation fluid. Wingate (1975) determined similar findings and concluded that bile acids

inhibitory action on human jejunum, ileum and colon is readily reversible when the bile acid is removed and that the unique value of the conjugated bile acids as experimental substances is that these are achieved with very low concentrations which only alter the osmotic and ionic differences between lumen and plasma by insignificant amounts. The ready reversibility of bile actions wherein the tissues resume abrupt full contractility suggests its relative intoxicity and the likelihood of membrane or surface activity, this is particularly apparent on aorta where after several experimentation with the same tissue, contractility need not necessarily be reinstituted indicating the removal of bile and the persistence of residual catecholamine after washing. This is also on agreement with the observation by Wingate *et al.* (1973) that bile acids disrupt cell membrane and Mekhjian *et al.* (1971) who stated that bile acids are surface active molecules that impair active sodium transport by altering enzymes configuration, binding competitively with binding phosphate or by altering lipoprotein interactions at cellular membrane. However, these investigators observed a potential cyto-toxicity of the fecal water-insoluble lithocholic acid. This was practically indemonstrable in the present research considering that this acid is produced by microflora by bacterial 7 dehydroxylation of the chenodeoxycholic acid component of bile. This is not different from the findings by Duane and Wiegani (1980) that by dissolution of mucosal lipids bile acids disrupt the gastric mucosal barrier. However, the findings by Forte *et al.* (1976) that the exposure of the serosal surface of the isolated bullfrog gastric mucosa to bile acids causes definite changes in histological and electrical characteristics of the tissue are in general disagreement with the present research and can be justified by the fact that these histo-pathological changes involved gastric serosal surface of an amphibian not a mammal.

In the present research, it has been demonstrated that bile is washable from the tissues, actions were reversible and no tissue damage was observed. These findings are consistent with the statement by Hofmann (1999) that bile acids are cytotoxic only when present in abnormally high concentrations that their conjugation in the liver to taurine and glycine renders them impermeable to cell membrane in the intestine and that bile acid therapy involves replacement therapy in deficiency states and the use of ursodeoxycholic acid in the protection of the hepatocytes from cholestatic injury. In a similar statement, Podda *et al.* (1982) endorsed their observation that a combination of chenodeoxycholate and ursodeoxycholate was more effective than either alone in reducing biliary cholesterol saturation. This is in general agreement with the assumption that whole bile might has better therapeutic efficacy than bile acids. The present investigation is not in disagreement with (Buchbinder, 1928) induction of bradycardia in puppies by ligation of common bile duct induction of cardiac standstill by bile salt administration and the usual clinical observation of bradycardia in patients with obstructive jaundice (Bockus, 1953). The demonstration of the antispasmodic effect of Ox bile on intestinal tissues in the present research not consistent with the finding of Wedlake *et al.* (2009) that idiopathic bile acid malabsorption prevailed in patients diagnosed with diarrhea-predominant Irritable Bowel Syndrome (IBS-D), Ford (2010) questioned the applicability of these findings due to the small sample size, the diagnosis based on clinical criteria ignoring potential underlying organic etiology and the fact that most recent reviews and meta-analysis demonstrated the prevalence of coeliac disease and small intestinal bacterial overgrowth in patients meeting the diagnostic criteria for IBS-D. The present vaso-dilatory findings are not in disagreement with the use of Bile Acid Sequestrants (BAS) in the treatment of coronary stenosis. Bays and Jones (2007) reported that BAS in monotherapy or with other lipid altering drugs decreased the incidence of coronary heart disease, decreased progression and increased regression of coronary atherosclerotic lesions with stenosis by improving removal of excessive hepatic and blood cholesterol also they decreased blood glucose in type 2 diabetes mellitus by a largely unknown mechanism.

## CONCLUSION

The *in vitro* Ox bile pharmacologic actions on isolated tissue preparations were determined. It is concluded that Ox bile exerts a pharmacodynamic actions that abolishes spontaneous and induced contractions of these tissues. The prompt onset at relatively low doses, suggests the membranous, contact, mechanism of these actions. The rapid resuming of contractility suggests the intoxicity and the affliction of no histo-pathologic changes by the substance. It may be justifiable to conduct future research towards further elucidation of bile pharmacokinetics with a view to utilizing its spasmolytic, vasodilatory and utero-spasmolytic actions.

## REFERENCES

Abdelhalim, S.E.A., 2004. A pharmacoligical study of the assumed intoxication by camel liver consumption. M.Sc. Thesis, University of Khartoum, Sudan.

Bays, H. and P.H. Jones, 2007. Colesevelam hydrochloride; reducing atherosclerotic coronary heart disease risk factors. Vasc. Health Risk Manage., 3: 733-742.

Bockus, H.L., 1953. Affections of the gallbladder and bile ducts, Gastro-entrologly. Philadelphia, 3: 424-715.

Boura, A., 1954. Improved automatic apparatus for pharmacological assays on isolated preparations. Br. J. Pharmacol., 9: 24-30.

Buchbinder, W.C., 1928. Experimental obstructive Jaundice. III. Age factor in the production of bradycardia. Arch. Int. Med., 42: 743-743.

Collee, J.G., A.G. Fraser, B.P. Marmion and A. Simmons, 1996. Practical Medical Microbiology. 14th Edn., Churchill Livingstone, New York, pp: 131-149.

Duane, W.C. and D.M. Wiegani, 1980. Mechanism by which bile salt disrupts the gastric mucosal barrier in the dog. J. Clin. Inves., 66: 1044-1049.

Forchgott, R.F. and S. Bhadrakom, 1953. Reactions of strips of rabbit aorta to epinephrine, isoproterenol, sodium nitrite and other drugs. J. Pharmacol. Exp. Ther., 108: 129-143.

Ford, A.C., 2010. Applicability of the reported prevalence of bile acid malabsorption in irritable bowel. Aliment. Pharmacol. Ther., 31: 161-162.

Forte, T.M., W. Siten and J.C. Forte, 1976. Ultrastructural Lesions in Gastric Mucosa Exposed to Deoxycholate: Implications Towards the Barrier Concept. In: Gastric Hydrogen Ion Secretion, Kasbekar, D.K., C. Sachs and W.S. Rehm, (Eds.), Marcel Dekker, Inc., New York, pp: 1-28.

Hofmann, A.F., 1999. The continuing importance of bile acids in liver and intestinal disease. Arch. Intern. Med., 159: 2647-2658.

Krebs, H.A. and K. Henseleit, 1932. Untersuchungen uber die harnstoff bildung in tierkorper. Hoppe-Seyler's Z. Physiol. Chem., 210: 33-66.

Mekhjian, H.S., S.F. Phillips and A.F. Hofmann, 1971. Colonic secretion of water induced by bile acids, perfusion studies in man. J. Clin. Inves., 50: 1569-1577.

Podda, M., M. Zuin, M.L. Dioguardi, S. Festurazzi and N. Dioguardi, 1982. A combination of chenodeoxycholic acid and ursodeoxycholic acid is more effective than either alone in reducing biliary cholesterol saturation. Hepatology, 2: 334-339.

Rampone, A.J., 1972a. Bile salt and non-bile salt components in bile affect cholesterol uptake by rat intestine *in vitro*. J. Physiol., 227: 889-898.

Rampone, A.J., 1972b. The effect of bile salt and raw bile on the intestinal absorption of micellar fatty acid in the rat *in vitro*. J. Physiol., 222: 679-690.

Thompson, E.B., 1990. Drug Bioscreening: Drug Evaluation Techniques in Pharmacology. VCH Publishers, inc., New York, USA, Pages: 195.

Thompson, F.N., 2001. Hormones affecting reproduction. Veterinary Pharmacol. Thera., 31: 612-625.

Tigani, H., 1969. A study of the pharmacology of the alimentary tract of the domestic fowl. Ph.D. Thesis, University of Edinbourgh, UK.

University of Edinburgh, Department of Pharmacology, 1970. Pharmacological Experiments on Isolated Preparations; Preparation of Physiological Salt Solutions. 2nd Edn., Churchill Livingstone, New York, pp: 92-95.

Wedlake, L., R. A'Hern, D. Russell, K. Thomas, J.R.F. Walters and H.J.N. Andreyev, 2009. Systematic review: The prevalence of idiopathic bile acid malabsorption as diagnosed by SeHCAT in patients with diarrhea-predominant irritable bowel syndrome. Aliment. Pharmacol. Thera., 30: 707-717.

Wingate, D.L., 1975. Bile Acids and Bulk Flow. Blackwell Press, New York.

Wingate, D.L., F.S. Phillips and A. Hofmann, 1973. Effect of glycine-conjugated bile acids with and without lecithin on water and glucose absorption in perfused human Jejunum. J. Clin. Inves., 52: 1230-1236.