International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
DOI: 10.22192/ijarbs Coden: IJARQG(USA) Volume 5, Issue 10 - 2018

Research Article

DOI: http://dx.doi.org/10.22192/ijarbs.2018.05.10.015

Anti-ulcerogenic Activity of a Polyherbal Formulation (EXR-HF) on Experimental Ulcer Models

ISERHIENRHIEN Lucky Osafanme[1*], AGATEMOR Uzuazokaro Mark- Maria[2], IDAKWOJI Precious Adejoh[3], NWEJE- ANYALOWU Paul Chukwuemeka[4], ONUGWU Ernest Okonkwo[5]

[1] Department of Biology, Faculty of Science, Nigeria Maritime University, Okerenkoko, Delta State, Nigeria
[2] Department of Biochemistry, Faculty of Biological Sciences, University of Nigeria, Nsukka, Enugu State, Nigeria
[3] Department of Biochemistry, Faculty of Natural Sciences, Kogi State University, Anyigba, Kogi State, Nigeria
[4] Department of Biochemistry, Faculty of Science, Clifford University, Owerrinta, Abia State, Nigeria
[5] Department of Biochemistry, College of Natural and Applied Sciences, Salem University, Lokoja, Kogi State, Nigeria
***Corresponding author: ISERHIENRHIEN Lucky Osafanme**
E-mail: *luckycheif@gmail.com*

Abstract

In this study we developed and evaluated four polyherbal formulations (EXR- HF_1, EXR- HF_2, EXR- HF_3 and EXR- HF_4) comprising of varying proportions of the aqueous extracts of *Anogeissus leiocarpus, Alchornea cordifolia, Persea americana* and *Tamarindus indica* leaves on indomethacin, ethanol and histamine ulcer models with the aim of investigating the anti-ulcer potentials of the formulations and also to identify the combination ratio with the highest potency. The result of the study showed that the polyherbal formulations displayed gastroprotective activity as demonstrated by significant ($P< 0.05$) inhibition of the formation of ulcers induced through the three different ulcer models. Furthermore, it was observed that among the polyherbal formulations, EXR-HF_4 exhibited the highest potency against ulcer. It was concluded that EXR-HF_4 can be used as an alternative to the orthodox anti- ulcer drugs or as an add-on therapy.

Keywords: polyherbal formulations, aqueous extracts, ulcer models, EXR-HF.

1.0 Introduction

Peptic ulcer is a term used to describe a group of ulcerative disorders that occur in areas of the upper gastrointestinal tract, which are exposed to acidic secretions and pepsin. It represents a chronic health problem. Approximately 10% of the population have or will develop peptic ulcer. Its incidence is slightly higher in men than women (1.3: 1) and although it occurs at any age, duodenal ulcer occurs most often in the range of 30–55 years, whereas gastric ulcer occurs in the range of 50–70 years (Rubin and Palazzo, 2006).

Although there is a large arsenal of drugs with antiulcerogenic activity on the market, none produces 100% remission of ulcers, with reduced side effects and without compromising the patient's wellbeing, which usually results in chronic use of these drugs. Studies have reported the widespread use of herbs and polyherbal formulations with antiulcerogenic properties. This global upsurge in the use of herbs and herbal products is largely due to the wide acceptability; accessibility and affordability of these herbs/ herbal products (Idakwoji and Uzuazokaro, 2018b). Polyherbal formulations are mixtures of many plant parts (which could be roots, leaves, stem, flowers, pods and seeds) obtained from various plant species and families (Idakwoji and Uzuazokaro, 2018a). These plants/ their combinations usually contain an array of bioactive compounds making them suitable for the treatment and management of a variety of disease conditions (Pieme *et al.*, 2006). This study was aimed at developing and evaluating a polyherbal formulation for its anti- ulcer activity. Four (4) polyherbal formulations namely EXR-HF (1-4) where prepared by mixing different proportions of the aqueous extracts of *Anogeissus leiocarpus*, *Alchornea cordifolia*, *Persea americana* (PA) and *Tamarindus indica* leaves.

Anogeissus leiocarpus (DC) Guill and Perr family Combretaceae (Common name: Axlewood tree) has many applications in Nigeria. *A. leiocarpus* is used medically for the treatment of ascaricide, gonorrhoea, general body pain, blood clots, asthma, coughing and tuberculosis (Mann *et al.*, 2003). Information obtained from the Yorubas and South-Eastern people of Nigeria illustrate that the plant is also used as an antimicrobial agent against bacterial infections (Dweek, 1996). The leaves of the plant are used externally as a decoction in the eastern part of Nigeria for the treatment of skin diseases and the itch of psoriasis. The powdered bark is applied to wounds, sores, boils, cysts and diabetic ulcers with good results. The powdered bark has also been mixed with 'green clay' and applied as an unusual face mask for serious blackheads (Dweek, 1996). The infusion and decoctions are used as cough medicine, the pulped roots are applied to wounds and ulcers, the powdered bark is also rubbed to reduced tooth ache on gums, it is also used as vermifuges and the leaves decoction is used for washing and fumigation (Ibrahim et al., 1997). *A. leiocarpus* is traditionally acclaimed to be effective in treating infectious wounds in man and animals (Dweek, 1996).

Alchornea cordifolia belongs to the family Euphorbiaceae and is distributed in secondary forests usually near water, moist or marshy places. It grows to a considerable height but is always of a shrubby or scrambling habit. It has long stalked cordate leaves and flowers in hanging racemes about one foot long (Dalziel, 1956). The antimicrobial properties of crude extracts prepared from plants have been reported (Hassan *et al.*, 2006; Kubmarawa *et al.*, 2007). *A. cordifolia* leaf extracts have been reportedly used in various African countries such as Senegal in the treatment of venereal diseases, conjunctivitis, dermatoses, stomach ulcers, bronchitis, cough, toothache (Le Grand and Wondergem, 1987; Le Grand, 1989) and Zaire in the treatment of urinary tract infection, infected wound, diarrhoea, cough, dental caries, chest pain and anaemia (Kambu *et al.*, 1990; Muanza *et al.*, 1994). In Sierra Leone it was used for diarrhoea and piles (Dalziel, 1956; Macfoy and Sama, 1990) and in Nigeria for gonorrhoea, yaws, rheumatic pain and cough (Gbile and Adeshina, 1986; Ogungbamila and Samuelson, 1990). Extracts from leaves of *A. cordifolia* have been reported to inhibit the growth of bacteria such as *Staphylococcus aureus*, *S. albus*, *Escherichia coli*, *Bacillus sp* and *Pseudomonas aeruginosa* (Ogunlana and Ramastad, 1975; Ebi, 2001). Anti-inflammatory activities of *A. cordifolia* have also been reported (Osadebe and Okoye, 2003; Manga *et al.*, 2004; Mavar-Manga *et al.*, 2008). Many plants synthesize substances that are useful to the maintenance of health in humans and animals (Lai and Roy, 2004).

Persea americana mill (Lauraceae) commonly called Avocado is a medium sized, erect and deciduous tree ranging from 15-20 m in height (Ojewole *et al*., 2007). Different parts of the plant are used in folk medicine for the treatment of several ailments such as hypertension, diabetes, inflammation, etc. (Gill, 1992; Adeyemi *et al*., 2002; Lans, 2006; Bartholomew *et al*, 2007). Specifically the fruit is used as vermifuge, for treatment of dysentery and as aphrodisiac (Watt &

Breyer-Brandwijk, 1962; Bartholomew *et al*., 2007). The leaves are used extensively in the treatment of hypertension (Gill, 1992; Lans 2006), sore throat, haemorrhage and inflammatory conditions (Bartholomew *et al*., 2007). Some of the scientifically validated activities of the plant leaves include its antihypertensive activity (Owolabi *et al*., 2005; Ojewole *et al*., 2007), anticonvulsant effect (Ojewole & Amabeoku, 2006), analgesic and anti-inflammatory activities (Adeyemi *et al*., 2002).

Tamarindus indica is leguminous trees of genus Tamarindus which is monotypic with only species indicum (Bently and Trimen, 2004). Tamarindus indica having family Fabaceae and sub-family Caesalpinaceae is a tropical evergreen tree native to Africa and Southern Asia (Kirtikar and Basu, 1987). Its various parts such as seeds, root, leaves, bark and fruits have been extremely used in traditional India and African medication (Gunasena, 2000). For years, tamarind has proven to be particularly useful for treating liver and gall disorders and has been studied severally on the role it plays in treating bile problems. Tamarind is particularly useful for managing pain and inflammation on joints. It has been seen that leaves and pulp crushed and applied on swollen joints provides great relief and reduces inflammation. Tamarind used for treating sore throat. It is either gargled or drunk as tamarind juice to help relief pain and discomfort of sore throats (Vyas, 2009; Asase, 2005). In Northern Nigeria, the fresh stem bark and leaves are used as decoction variegated with potash for the treatment of stomach disorder, general body pain, jaundice, yellow fever and as a blood tonic and skin cleanser (Komatarin and Azadi, 2004). Various parts have been expansively studied in terms of the pharmacological activity potent antibacterial, antifungal, hypoglycaemic, cholesterolemic (Khazandi *et al.*, 2008), hypolipidemic, antioxidant (Tsuda *et al.*, 1994), antihepatotoxic, anti-inflammatory (Rimbau *et al.*, 1999), and antidiabetic (Maiti *et al.*, 2004) properties.

Due to the rich pharmacological profiles of *Anogeissus leiocarpus, Alchornea cordifolia, Persea americana* and *Tamarindus indica*, in this study we developed and evaluated four polyherbal formulations comprising of varying proportions of these plants on indomethacin, ethanol and histamine ulcer models with a few of investigating the anti-ulcer potentials of the formulations and also to identify the combination ratio with the highest potency.

2.0 Materials and Methods

2.1 Materials

2.1.1 Chemicals and drugs

All chemicals used in this study were of analytical grade and were purchased from Sigma Chemical Co. Ltd (USA) through a local vendor. Propranolol, Cimetidine and Indomethacin were purchased from a local pharmacy shop.

2.1.2 Animals

Male adult wistar rats weighing 150–200g were used for this study. They were kept in stainless steel cages under standard laboratory conditions. They were maintained on clean water and standard rodent feed.

2.2 Methods

2.2.1 Plant Collection and Identification

The leaves of *Anogeissus leiocarpus, Alchornea cordifolia, Persea americana and Tamarindus indica* were collected from a natural habitat in Idah Area of Kogi State, Nigeria. The plants were identified at the herbarium unit of Biological Sciences Department, Federal University, Lokoja and voucher specimens were deposited for future references.

2.2.2 Preparation of Extracts/ Polyherbal Formulation

The leaves of each of the plants were shade- dried for five (5) days and pulverized using an electric blender. One thousand and five hundred (2000) gram of each of the pulverized leaves was soaked separately in distilled water for 72- hours. The resulting mixtures were filtered using Whatmann filter paper (Size No1) and the extracts were concentrated using a free- dryer. Four (4) polyherbal formulations namely EXR-HF (1-4) where prepared by mixing the extracts in the following proportions:

EXR-HF_1- (1 part *Anogeissus leiocarpus,* 1 part *Alchornea cordifolia,* 2 parts *Persea americana* and 1 part *Tamarindus indica*)
EXR-HF_2- (1 part *Anogeissus leiocarpus,* 2 parts *Alchornea cordifolia,* 1 part *Persea americana* and 1 part *Tamarindus indica*)

EXR-HF_3- (2 parts *Anogeissus leiocarpus*, 1 part *Alchornea cordifolia*, 1 part *Persea americana* and 2 parts *Tamarindus indica*)
EXR-HF_4- (1 part *Anogeissus leiocarpus*, 1 part *Alchornea cordifolia*, 1 part *Persea americana* and 2 parts *Tamarindus indica*)

2.2.3 Acute Toxicity Study

The oral median lethal dose (LD50) of the polyherbal formulations was determined in rats according to the method of Lorke (1983).

2.2.4 Evaluation of antiulcer activity

2.2.4.1 Indomethacin-induced ulceration

Male adult albino rats were used for the experiment. They were randomly divided into 6 groups of 5 rats each. Food was withdrawn 24 h and water 2 h before the commencement of the experiment (Alphin and Ward, 1967). Group 1 (control) received only indomethacin (Sigma, 60 mg/kg p.o. dissolved in 5% Na_2CO_3); Groups 2 - 5 were pretreated with 400mg/ kg p.o of EXR- HF_1, EXR- HF_2, EXR- HF_3 and EXR- HF_4 respectively. Group 6 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80). One hour later, groups 2-5 were administered indomethacin. Four hours after indomethacin administration, animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al.*, 1996). Ulcer index (UI) and preventive ratio (PR) of each of the groups pretreated with extract was calculated using standard methods (Zaidi and Mukerji, 1985; Nwafor *et al.*, 2000).)

2.2.4.2 Ethanol-induced gastric ulceration

The procedure was similar to that used in indomethacin induced ulceration. The rats randomly assigned into 6 groups of 5 rats each based on their body weight. Food was withdrawn 24 h and water 2 h before the commencement of experiment (Alphin and Ward, 1967). Group 1 (control) received only ethanol (2.5 ml/kg p.o), Groups 2 - 5 were pretreated with 400mg/ kg p.o of EXR- HF_1, EXR- HF_2, EXR- HF_3 and EXR- HF_4 respectively, Group 6 received propranolol (40 mg/kg p.o. dissolved in distilled water). One hour later, groups 2- 6 were administered ethanol. Four hours after ethanol administration, animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al.*, 2000).

2.2.4.3 Histamine-induced gastric ulceration

Rats were randomized into 6 groups of 5 rats each. Food was withdrawn 24 h and water 2h before the commencement of experiment (Alphin and Ward, 1967). Group 1 (control) received only histamine acid phosphate (Sigma, 100mg/kg i.p. dissolved in distilled water) (Maity *et al.*, 1995); Groups 2 – 5 were pretreated with 400mg/ kg p.o of EXR- HF_1, EXR- HF_2, EXR- HF_3 and EXR- HF_4 respectively; Group 6 received cimetidine (100 mg/kg p.o. dissolved in 50% Tween 80), 1 hour prior to histamine administration. One hour later, groups 2-5 were administered with histamine acid phosphate (100mg/kg, i.p). 18 hours after histamine administration, animals were killed by cervical dislocation. The stomachs were removed and opened along the greater curvature. The tissues were fixed with 10% formaldehyde in saline. Macroscopic examination was carried out with a hand lens and the presence of ulcer lesion was scored (Nwafor *et al.*, 1996). Ulcer indexes (UI) and preventive ratio (PR) of each of the groups pretreated with the extract were calculated using standard methods (Zaidi and Mukerji, 1985; Nwafor *et al.*, 2000).

2.2.5 Statistical Analysis

Statistical analysis was carried out using SPSS version 20.0. All the data were expressed as mean ± SEM and the statistical differences between the means were determined by one way analysis of variance (ANOVA) which was followed by Turkey-Kramer multiple comparison and difference between means at $P > 0.05$ were considered significant.

3.0 Results

3.1 Acute Toxicity

The results of acute toxicity studies showed no sign of toxicity or mortality up to a dose of 5000 mg/kg of the polyherbal formulations (Table 1). The oral LD_{50} was then taken to be > 5000 mg/kg for each of the formulations.

Table 1: Observed Effects of the Polyherbal Formulations on Rats

Phase	Group	Treatment (mg/kg)	D/T	Observed Sign of Toxicity
I	1	EXR- PF_1 (10)	0/3	-
	2	EXR- PF_1 (100)	0/3	-
	3	EXR- PF_1 (1000)	0/3	-
II	1	EXR- PF_1 (1600)	0/1	-
	2	EXR- PF_1 (2900)	0/1	-
	3	EXR- PF_1 (5000)	0/1	-
I	1	EXR- PF_2 (10)	0/3	-
	2	EXR- PF_2 (100)	0/3	-
	3	EXR- PF_2 (1000)	0/3	-
II	1	EXR- PF_2 (1600)	0/1	-
	2	EXR- PF_2 (2900)	0/1	-
	3	EXR- PF_2 (5000)	0/1	-
I	1	EXR- PF_3 (10)	0/3	-
	2	EXR- PF_3 (100)	0/3	-
	3	EXR- PF_3 (1000)	0/3	-
II	1	EXR- PF_3 (1600)	0/1	-
	2	EXR- PF_3 (2900)	0/1	-
	3	EXR- PF_3 (5000)	0/1	-
I	1	EXR- PF_4 (10)	0/3	-
	2	EXR- PF_4 (100)	0/3	-
	3	EXR- PF_4 (1000)	0/3	-
II	1	EXR- PF_4 (1600)	0/1	-
	2	EXR- PF_4 (2900)	0/1	-
	3	EXR- PF_4 (5000)	0/1	-

Key: D= Number of deaths, T= Number of treated animals

3.2 Indomethacin-induced Gastric Ulceration

Table 2 shows that indomethacin induced gastric ulcer in all experimental groups. Groups treated with the polyherbal formulations (EXR-HF_1, EXR- HF_2, EXR-HF_3 and EXR-HF_4) had significant reduction ($p < 0.05$) in the gastric erosions formed compared to control as evident in the reduction of ulcer indices. The potency of the formulations in reducing ulcer varied considerably. EXR-HF_4 showed 94. 63% inhibition of ulcer, which was comparable to that of cimetidine, the anti-ulcer drug used, which had 95.16% inhibition, while EXR-HF_1, EXR- HF_2 and EXR-HF_3 showed 77.39, 85.99 and 58.59% inhibition respectively.

Table 2 Effect of the Polyherbal Formulations on Indomethacin-induced Gastric Ulcer

Treatment (mg/kg)	Ulcer Index	% Ulcer Inhibition
Control (Indomethacin 60 mg/kg)	17.34±1.46	-
EXR-HF_1 (400 mg/kg)	3.92±1.06*	77.39
EXR-HF_2 (400 mg/kg)	2.43±0.94*	85.99
EXR-HF_3 (400 mg/kg)	7.18±1.33*	58.59
EXR-HF_4 (400 mg/kg)	0.93±0.21*	94.63
Cimetidine(100 mg/kg)	0.84±0.16*	95.16

Data were expressed as mean ± SEM. significant at *P < 0.05 when compared to control n = 5.

3.3 Ethanol- induced Gastric Ulceration

As shown in Table 3, ethanol induced gastric ulcer in all the experimental groups. Groups treated with the polyherbal formulations (EXR-HF_1, EXR- HF_2, EXR-HF_3 and EXR-HF_4) also had significant reduction ($p < 0.05$) in the gastric erosions formed compared to control. This was evident in the reduction of ulcer indices. The potency of the formulations in reducing the ethanol- induced ulcer also showed variations. EXR-HF_4 showed the maximum (100 %) inhibition of ulcer while which was more than that of propranolol which had 91.54% inhibition, while EXR-HF_3 showed the lowest (43.90%) inhibition. EXR-HF_1 and EXR-HF_2 showed 63.90 and 68.62% inhibition respectively.

Table 3 Effect of the Polyherbal Formulations on Ethanol- induced Gastric Ulcer

Treatment (mg/kg)	Ulcer Index	% Ulcer Inhibition
Control (Ethanol)	6.15±1.18	-
EXR-HF_1 (400 mg/kg)	2.22±0.98*	63.90
EXR-HF_2 (400 mg/kg)	1.93±0.66*	68.62
EXR-HF_3 (400 mg/kg)	3.45±1.01*	43.90
EXR-HF_4 (400 mg/kg)	0.00±0.00*	100.00
Propranolol (40 mg/kg)	0.52±0.11*	91.54

Data were expressed as mean ± SEM. significant at *P < 0.05 when compared to control n = 5.

3.4 Histamine– induced Ulceration

Table 2 shows that Histamine induced gastric ulcer in all experimental groups. Groups treated with the polyherbal formulations (EXR-HF_1, EXR- HF_2, EXR-HF_3 and EXR-HF_4) equally had significant reduction ($p < 0.05$) in the gastric erosions formed compared to control as evident in the reduction in the ulcer indices. EXR-HF_4 showed 95. 23% inhibition of ulcer, which was comparable to that of cimetidine, the anti-ulcer drug used, which had 96.59% inhibition, while EXR-HF_1, EXR- HF_2 and EXR-HF_3 showed 78.20, 92.05 and 68.51% inhibition respectively.

Table 4 Effect of the Polyherbal Formulations on Histamine-induced Gastric Ulcer

Treatment (mg/kg)	Ulcer Index	% Ulcer Inhibition
Control (Histamine 100 mg/kg)	13.21±1.23	-
EXR-HF_1 (400 mg/kg)	2.88±0.98*	78.20
EXR-HF_2 (400 mg/kg)	1.05±0.71*	92.05
EXR-HF_3 (400 mg/kg)	4.16±1.01*	68.51
EXR-HF_4 (400 mg/kg)	0.63±0.11*	95.23
Cimetidine(100 mg/kg)	0.45±0.14*	96.59

Data were expressed as mean ± SEM. significant at *P < 0.05 when compared to control n = 5.

4.0 Discussion

Polyherbal formulations are mixtures of many plant parts (which could be roots, leaves, stem, flowers, pods and seeds) obtained from various plant species and families. These plants/ their combinations usually contain an array of bioactive compounds making them suitable for the treatment and management of a variety of disease conditions (Pieme *et al.*, 2006). It is generally believed that polyherbal formulations are just effective as the conventional drugs or more potent against diseases when taken alongside conventional drugs. By using herbal combinations, nature provides a balance of ingredients that may act as buffers, synergists or counterbalances, which work in harmony to rid the body of diseases and infirmities (Montrale, 1998). Some polyherbal extracts have been scientifically proven for efficacy in the treatment of diseases while many others are yet to be investigated (Idakwoji *et al.*, 2016).

In this study we developed and evaluated four polyherbal formulations (EXR- HF_1, EXR- HF_2, EXR-HF_3 and EXR- HF_4) comprising of varying proportions of *Anogeissus leiocarpus*, *Alchornea cordifolia*, *Persea americana* and *Tamarindus indica* on indomethacin, ethanol and histamine ulcer models with a few of investigating the anti-ulcer potentials of the formulations and also to identify the mixing proportion with the highest potency.

Indomethacin is known to cause ulcer especially in an empty stomach (Bhargava *et al*., 1973) and mostly on the glandular (mucosal) part of the stomach (Evbuonwa and Bolarinwa, 1990; Nwafor *et al*., 1996) by inhibiting prostaglandin synthetase through the cycloxygenase pathway (Rainsford, 1987). Prostaglandins function to protect the stomach from injury by stimulating the secretion of bicarbonate and mucus, maintaining mucosal blood flow and regulating mucosal turn over and repair (Hayllar and Bjarnason, 1995; Hiruma-Lima *et al*., 2006). This suppression of prostaglandins synthesis by indomethacin results in increased susceptibility of the stomach to mucosal injury and gastro-duodenal ulceration. The polyherbal formulations were observed to significantly reduce mucosal damage in the indomethacin– induced ulcer model, suggesting the possible extract mobilization and involvement of prostaglandin in the anti- ulcer effect of the extract. The potency of the formulations in reducing ulcer varied considerably. EXR-HF_4 showed the highest (94. 63%) inhibition of ulcer, which was comparable to that of cimetidine, the anti-ulcer drug used, which had 95.16% inhibition, while EXR-HF_1, EXR- HF_2 and EXR-HF_3 showed 77.39, 85.99 and 58.59% inhibition respectively. The implication of this is that, EXR-HF_4 can be an alternative to cimetidine or used as an adjunct in a therapeutic regimen.

Ethanol has been reported to cause disturbances in gastric secretion, damage to the mucosa, alterations in the permeability, gastric mucus depletion and free radical production (Salim, 1990). This is attributed to the release of superoxide anion and hydroperoxy free radicals during metabolism of ethanol as oxygen derived free radicals has been found to be involved in the mechanism of acute and chronic ulceration in the gastric mucosa (Pihan *et al*.,1987). It was also observed in this study that the polyherbal formulations significantly reduced ethanol induced ulcer. This may be due to cytoprotective effect of the extract via antioxidant effects. Ethanol is also reported to cause gastric mucosal damage by stimulating the formation of leukotriene C4 (LTC4) (Whittle *et al*.,1985).The gastroprotective effect of the formulations may in part be due to the suppression of lipoxygenase activity (Nwafor *et al*.,1996). The potency of the formulations in reducing the ethanol- induced ulcer also showed variations. EXR-HF_4 again showed the maximum (100 %) inhibition of ulcer which was more than that of propranolol which had 91.54% inhibition, while EXR-HF_3 showed the lowest (43.90%) inhibition. EXR-HF_1 and EXR- HF_2 showed 63.90 and 68.62% inhibition respectively.

Histamine-induced ulceration is known to be mediated by enhanced gastric acid secretion as well as by vasospastic action of histamine (Cho and Pfeiffer, 1981). The inhibition of ulcer due to histamine by the extract may be due to its suppression of histamine-induced vasospastic effect and gastric secretion. Antioxidants such as quercetin have been reported to prevent gastric mucosal lesions in various experimental models (Di Carlo *et al*., 1999; Zayachkivska, 2005) by increasing the amount of neutral glycoproteins (Di Carlo *et al*., 1999). Antioxidants such as flavonoids have been reported to protect the gastric mucosa from damage by increasing the mucosal prostaglandin content and by inhibiting histamine secretion from mast cells by inhibition of histidine decarboxylase. Free radical scavenging ability of flavonoids has been reported to protect the gastrointestinal tract from ulcerative and erosion lesion (Borrelli and Izzo, 2000). Saponins, especially triterpenes type have been implicated in antiulcer activity mediated by formation of protective mucus on the gastric mucosa and also protect the mucosa from acid effects by selectively inhibiting PGF2α (Agwu and Okunji, 1986; Lewis and Hanson, 1991). The high antioxidant activity of the individual component plants of the polyherbal formulations therefore must have been responsible for the observed gastroprotective potentials. EXR-HF_4 again showed the highest (95. 23%) inhibition of ulcer, which was comparable to that of cimetidine, the anti-ulcer drug used, which had 96.59% inhibition, while EXR-HF_1, EXR- HF_2 and EXR-HF_3 showed 78.20, 92.05 and 68.51% inhibition respectively.

5.0 Conclusion

In conclusion, the results of the present study show that the polyherbal formulations display gastroprotective activity as demonstrated by the significant inhibition of the formation of ulcers induced through the three different ulcer models studied. Furthermore, it was observed that among the polyherbal formulations, EXR-HF_4 (1 part *Anogeissus leiocarpus*, 1 part *Alchornea cordifolia*, 1 part *Persea americana* and 2 parts *Tamarindus indica*) exhibited the highest potency against ulcer formation. The implication of this is that EXR-HF_4 can be used as an alternative to the orthodox anti- ulcer drugs or as an add-on therapy.

References

Adeyemi, O. O., Okpo, S. O. and Ogunti, O. O. 2002. Analgesic and anti-inflammatory effects of the aqueous extract of leaves of *Persea Americana* mill (Lauraceae) *Fitoterapia*, 73: 375- 380.

Agwu, C. N., Okunji, C. O. 1986. Gastrointestinal studies of *Pyrenacantha staudtii* leaf extracts. *Journal of Ethnopharmacology* 15: 45 – 55.

Alphin, R. S. and Ward, J. W. 1967. Action of hexopyrronium bromide on gastric secretion in dogs and on gastric secretion and ulceration in rats. *Archives Internationales de Pharmacodynamie et de Therapie;* 6(15) 10-16

Asase, A., Oteng-Yeboah A. A, Odamtten G. T, and Simmonds, M. S. J. 2005. Ethnobotanical study of some Ghanaian antimalarial plants. *Journal of Ethnopharmacology*; 99: 273-279.

Bartholomew, I.C.B, Odetola, A. A. and Agomo, P. U. 2007. Hypoglycaemic and hypocholesterolemic potential of *Persea Americana* leaf extracts. *Journal of Medicinal Food*, 10: 356-360.

Bentley R. and Trimen, H 2004.:Medicinal Plants. Asiatic Publishing House New Delhi, Vol. 1, 20.

Bhargava, K. P., Gupta, M. B., Tangri, K. K. 1973. Mechanism of ulcerogenic activity of indomethacin and oxyphenbutazone. *European Journal of Pharmacology* 22: 191 – 195.

Borrelli, F. and Izzo, A. A. 2000. The plant kingdom as source of anti-ulcer remedies. *Phytotherapy Research* 14: 581 – 591.

Cho, C. H. and Pfeiffer, C. J. 1981. Gastrointestinal ulceration in the guinea pigs in response to dimaprit, histamine and H1 and H2 blocking agents. *Digestive Disease Science* 26:306 – 311.

Dalziel JM (1956). The Useful Plants of West Tropical Africa. ed 3, Crown Agents for Oversea Government and Administration. Millbank, London p. 455.

Di Carlo, G., Mascolo, N., Izzo, A. A. and Capasso, F. 1999. Flavonoids: old and new aspects of a class of a natural therapeutic drug. *Life sciences* 64: 337 – 353.

Dweek, A. A. 1996. Plant for Africa. Part 2 http://www.dweek data.Co.uk/published papers.

Ebi, C. 2001. Antimicrobial activities of *Alchornea cordifolia*. Fitoterapia. 72(1): 69-72.

Evbuonwa, M. T and Bolarinwa, A. F. 1990. Effect of diet on indomethacin-induced peptic ulceration in pregnant rats. *Nigerian Journal of Physiological Sciences* 6:189 – 191.

Gbile, Z. O. and Adeshina, S. K. 1986. Nigerian Flora and its Pharmaceutical Potentials. Mediconsult. 31: 7-16.

Gill, L.S. 1992. Ethnomedical Uses of Plants in Nigeria. Uniben Press Benin, Nigeria.

Gunasena, L. H. P. M. 2000. Hughes A: Tamarind. *Tamarindus indica*. International Centre for Underutilised Crops. 23-29

Hassan, S. W, Umar, R. A, Lawal M, Bilbis, L. S and Muhammad, B. Y. 2006.Evaluation of antifungal activity of *Ficus sycomorus* L. (moraceae). Biol. Environ. Sci. J. Tropics 3: 18-25.

Hayllar, J. and Bjarnason, I. (1995). NSAIDS, COX-2 inhibitor and the gut .*Lancet* 346 - 522.

Hiruma-Lima, C. A., Calvo, T. R., Rodriguez, C. M., Andrade, F. D. P., Vilegas, W. and Brito, ARM. 2006. Antiulcerogenic activity of *Alchornea castaneaefolia* effects on somatostatin, gastrin and prostaglandin. *Journal of Ethnopharmacology* 104: 215 – 224.

Ibrahim, M. B, Owonubi, M. O and Onaopo, J. A 1997. Antibacterial effect of extract of leaf, stem and roof bark of Anogeissus leiocarpus on some bacterial organisms. *J. Pharm. Res. Dev*. 2(1): 20-23.

Idakwoji, P. A, Akuba, O. B, Okafor, S. C. 2016. Comparative Anti-radical Activity of Five Indigenous Herbal Plants and their Polyherbal Extract. *Int J of Biochem Res Rev*; 11(1): 1-10.

Idakwoji, P. A. and Uzuazokaro, M. A. 2018a. Evaluation of Pharmacological Profile Of Koju®- A Nigerian Polyherbal Formulation, in Wistar Rats. *World Journal of Pharmaceutical Research*; 7 (2)158-176

Idakwoji, P. A. and Uzuazokaro, M. A. 2018b. Evaluation of Toxicogical Profile Of Koju®- A Nigerian Polyherbal Formulation, in Wistar Rats. *World Journal of Pharmaceutical Research*; 7 (2)122- 144

Kambu, K., Tona, L., Kaba, S., Cimanga, K., and Mukala, N. 1990. Antispasmodic activity of extracts proceeding of plant, antidiarrhoeic traditional preparations used in Kinshasa, *Zaire. Ann. Pharm. FR*. 48(4): 200-208.

Khanzada, S. K, Shaikh, W., Sofia, W., Kazi, T., Usmanghani, K., Kabir, A., Sheerazi, T. H 2008. Chemical constituents of *tamarindus indica*, Medicinal plant in sindh. *Pakistani Journal of Botany*; 40(6):2553-2559.

Kirtikar, K. R., Basu, B. D: Indian Medicinal Plants. Edition 3, Vol. II, 1987: 887-891.

Komutarin, T, Azadi S, Butterworth L, Keil D, Chitsomboon B, Suttaji M, Meade BJ: 2004. Extract of the seed coat of *Tamarindus indica* exhibits nitric oxide production by murine

microphages *in vitro* and *in vivo*. *Food Chemical Toxicology*; 42:649-658.

Kubmarawa, D, Ajoku, G. A, Enwerem, N. M, Okorie, D. A. 2007. Preliminary phytochemical and antimicrobial screening of 50 medicinal plants from Nigeria. *Afr. J. Biotechnol*. 6(14): 1690-1696.

Lai, P. K and Roy, J. 2004. Antimicrobial and chemopreventive properties of herbs ands spices. *Curr. Med. Chem.* 11(11): 1451-1460.

Le Grand, A. 1989. Anti-infectious phytotherapy of the tree-savannah, Senegal (West Africa) III; A review of the phytochemical substances and anti-microbial activity of 43 Species. *J. Ethnopharmacol.* 25(3): 315-338.

Le Grand, A. and Wondergem, P. A. 1987. Antiinfective Phytotherapy of the Savannah Forests of Senegal (East Africa), an Inventory. *J. Ethnopharmacol*. 21(2): 109-125.

Lewis, D. A., Hanson, D. 1991. Anti-ulcer drugs of plants origin. *Progress in Medicinal Chemistry* 28:208 – 210.

Lorke, D. 1983. "A new Approach to Practical Acute Toxicity Testing." *Archives of Toxicology* 54: 275-287.

Macfoy, C. A. and Sama, A. M. 1990. Medicinal plants in Pujehun District of Sierra Leone. *J. Ethnopharmacol.* 30(3): 610-632.

Maiti, R., Jana, D., Das, U. k, Hosh, D. 2004. Antidiabetic effect of aqueous extract of seed of *Tamarindus indica*L. in streptozotozin-induced diabetic rats. Journal of *Ethnopharmacology*; 92:85-91.

Manga, H. M, Brkic, D., Marie, D. E. P. and Leclercq Q. 2004. *In vivo* anti-inflammatory activity of *Alchornea cordifolia* (Schumach. and Thonn.) Mull. Arg. (Euphorbiaceae). *J. Ethnopharmacol*. 94: 209-214.

Manjunatha, B. K, Krishna, V., Vidya, S. M, Mankani, K. L. and Manohara, Y. N. 2007. Wound healing activity of *Lycopodium serratum*. *Indian J. Pharm. Sci.* 69(2): 283-287.

Mann, A, Gbate, M. and Umar N. A . 2003. Medicinal and economic plants from Nupe land. Jube-Evans Publisher. p. 67.

Montrale, J. 1998. Anti- radical and lipid peroxidative effects of some plant extracts used by Sri Lankan traditional medical practitioners for cardio-protection. *Phytother. Res*; 5: 519-523.

Muanza, D. N, Kim, B. W., Euter, K. L. and Williams L. 1994. Antibacterial and antifungal activities of nine medicinal plants from Zaire. *Int. J. Pharmacog*. 32(4): 337-345.

Nwafor, P. A., Effraim, K. D. and Jacks, T. W. 1996. Gastroprotective effects of aqueous extracts of Khaya *senegalensis* bark on indomethacin – induced ulceration in rats. *West African Journal of Pharmacology and Drug Research* 12:46 – 50.

Nwafor, P. A., Okwuasaba, F. K. and Binda, l. G. 2000. Antidiarrhoeal and antiulcerogenic effects of methanolic extracts of *Asparagus pubescens* root in rats. *Journal of Ethnopharmacology* 72:421 – 427.

Ogungbamila, F. O and Samuelson, G. 1990. Smooth muscle relaxing flavonoids from *Alchornea cordifolia*. Acta. Pharm. Nordica. 2(6): 421-423

Ogunlana, E. O and Ramstad, E. 1975. Investigations into the antibacterial activities of local plants. *Planta medica* 27: 354-355.

Ojewole, J. A. O., Kamadiyaapa, D. R., Gondwe, M. M., Moodley, K., Musabayane, C. T. (2007). Cardiovascular effects of *Persea Americana* Mill (Lauraeae) (avocado) aqueous leaf extract in experimental animals. *Cardiovascular Journal of South Africa*, 18: 69-76.

Osadebe, P. O. and Okoye, F. B. 2003. Anti-inflammatory effects of crude methanolic extract and fractions of *Alchornea cordifolia* leaves. *J. Ethnopharmacol*. 89(1): 19-24.

Owolabi, M. A., Jaja, S. I. and Coker, H. A. 2005. Vasorelaxant action of aqueous extract of the leaves of *Persea Americana* on the isolated thoracic rat aorta. *Fitoterapia* 76: 567-

Pieme, C. A., Penlap, V. N, Nkegoum, B., Taziebou, C. L, Tekwu, E. M, Etoa, F. X, Ngongang J.2006. Evaluation of acute and subacute toxicities of aqueous ethanolic extract of leaves of (L) Roxb (Ceasalpiniaceae). *Afr J Biotechnol*; 5(3): 283- 289.

Pihan G., Regillo, C., Szabo S. 1987. Free radicals and lipid peroxidation in ethanol or aspirin – induced gastric mucosa injury. *Digestive Diseases and Sciences*; 5(3): 23-24

Rainsford, K. D. 1987. The effects of 5- lipoxygenase inhibitors and leukotriene antagonists on the development of gastric lesions induced by nonsteroidal anti-inflammatory drugs in mice. *Agents and Action* 21:316 – 319.

Rimbau V, Cerdan C, Vila R, Iglesia J. 1999. Antiinflammatory activity of some extracts from plants used in traditional medicines of North-African countries (II). *Phytotherapy Research*; 13:128-132**.**

Rubin E. and Palazzo J. P. 2006.“Trato gastrointestinal,” in *Patologia: Bases Clinicopatol´ogicas*, E. Rubin, Ed., chapter 13, pp. 673–750, Guanabara Koogan, Rio de Janeiro, Brazil.

Salim, A. S. 1990. Removing oxygen derived free radicals stimulates healing of ethanol- induced erosive gastritis in the rats. *Digestion* 47: 24 – 28.

Tsuda, T., Watanable, M., Ohshima, K., Yamanato, A., Kawakishi, S. and Osawa T. 2009. Antioxidative components isolated from the seed of tamarind (*Tamarindus indica* L.). *Journal of agriculture and food chemistry*; 42:2671-1674.

Vyas, N., Gavatia, N. P, Gupta, B. 2009. Tailing M: Antioxidant potential of Tamarindus indica seed coant. *Journal of Pharmacy research*; 2(11):1705-1706.

Watt, J. M. and Breyer-Brandwijk, M. G. 1962. The Medicinal and poisonous plants of Southern and Eastern and Eastern Africa, 2nd edn. Edinburg: E & S Livingstone, pp 53-54.

Whittle, B. J. R., Oren-Wolman, N. and Guth, P. H. 1985. Gastric vasoconstrictor actions of leukotriene C4 and PGF2α and thromboxane mimetic (U-4669) on rats submucosal microcirculation *in vivo*. *American Journal of Physiology* 248: G580 – G586

Zaidi, S. H. and Mukerji, B. 1958. Experimental peptic ulceration. Part 1. The significance of mucus barrier. *Indian Journal of Medical Research* 46:27 – 37.

Zayachkivska, O. S., Konturek, S. J., Drozdowicz, D., Konturek, P. C., Brzozowski, T. and Ghegotsky, M. R. 2005. Gastroprotective effects of flavonoids in plants extracts. *Journal of Physiology and Pharmacology* 56: 216 - 231.

Access this Article in Online	
	Website: www.ijarbs.com
Quick Response Code	Subject: Biochemistry
DOI:10.22192/ijarbs.2018.05.10.015	

How to cite this article:
ISERHIENRHIEN Lucky Osafanme, AGATEMOR Uzuazokaro Mark- Maria, IDAKWOJI Precious Adejoh, NWEJE- ANYALOWU Paul Chukwuemeka, ONUGWU Ernest Okonkwo. (2018). Anti-ulcerogenic Activity of a Polyherbal Formulation (EXR-HF) on Experimental Ulcer Models. Int. J. Adv. Res. Biol. Sci. 5(10): 147-156.
DOI: http://dx.doi.org/10.22192/ijarbs.2018.05.10.015