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Research Article

In vivo Antiulcer Activity of Phospholipid–Based Complexes of *Musa Paradisiaca* (*Musaceae*) Peel Extract for Improved Oral Drug Delivery

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ABSTRACT

Many herbal extracts have excellent *in-vitro* activity but less *in-vivo* activity because of their macromolecular size and poor lipid solubility which resulted in poor absorption and bioavailability problems. Some of these challenges could be overcome through the formulation of novel drug delivery systems such as phytosomes. Phytosomes provide better absorption and bioavailability than the conventional herbal extracts. *Musa paradisiaca* phytosome complexes were formulated and evaluated with the following parameters: Percentage yield, phytochemical screening, morphology, drug content, FTIR, *in vitro* release studies and *in vivo* anti-ulcer activity. Results showed that the % yield was 60 % and contains some phyto constituents. Batch A had a significantly higher EE ($p < 0.05$) in the range of 77.00 ± 1.30 - 93.00 ± 2.80 than others, while the batch B was in the range of 49.00 ± 1.90 - 72.00 ± 1.60. In batch A, AK1 had a significant highest drug release ($p < 0.05$) of 85 %, while AK2 had the lowest drug release of 70 %, while in batch B, BC2 had the highest drug release of 65 %. *Musa Paradisiaca* phytosome complex formulated with Kolliphor® HS 15 exhibited more antiulcerogenic activity when compared to the pure extract and standard. Hence, *Musa paradisiaca* complexes (1:1) formulated with Kolliphor® HS 15 at 200 mg/kg serves as a potential antiulcer agent with an improved bioavailability than conventional formulations.

INTRODUCTION

Drug delivery is the method of formulation of a pharmaceutical compound to achieve a therapeutic effect in man for the treatment of human diseases. Many routes of drug delivery are gaining increasing importance in medicine. These routes provide promising alternatives to parenteral drug delivery particularly for peptide and protein therapeutics. For this purpose, several novel drug delivery systems have been formulated which include phytosome, liposomes, microspheres, gels, and solid dispersion among others. Some of these drug deliveries have been employed in the formulation of some drugs which include herbal extract.

Investigation of herbal products has tremendously contributed to the drug production and has provided novel chemical structures and new pharmacological activities.

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Herbal medicines containing bioactive constituents are mostly highly water soluble. They are not adequately miscible for an ideal bioavailability. The bioavailability of some orally administered botanical extracts is usually erratic and poor due to limited gastrointestinal absorption. Flavonoid is one of the water-soluble phytoconstituents and likely to be poorly absorbed due to the poor miscibility with oils and other lipids or due to their multiple-ring large size molecules which cannot be absorbed by simple diffusion. These factors limit its ability to pass across the lipid-rich outer membranes of the enterocytes of the small intestine. It has been reported that the ability of flavonoids to cross the lipid-rich outer membrane of small intestine enterocytes is critically limited [1, 2]. Bioavailability can be improved by using new drug delivery systems which can enhance the rate and the extent of solubilization into aqueous intestinal fluids and the capacity to cross biomembranes. Phospholipids based drug delivery systems have been found promising for

better and effective delivery of drug and it provides much appropriate systematic drug delivery. The lipid-phase substance employed to formulate phytoconstituents, are lipid compatible which include phospholipids from soy, mainly phosphatidylcholine. Phospholipids are complex molecules that are found in life as a component of cell membranes. The phospholipid molecular structure includes a water-soluble head and two fat-soluble tails, and because of this dual solubility, the phospholipid acts as an effective emulsifier. Complexing of the polyphenol (water-soluble phytoconstituents) in the molar ratio with phosphatidylcholine results into a new herbal drug delivery system known as phytosome. Phytosome is an advanced herbal technology that offers improved absorption, enhanced delivery and increased bioavailability of medicinal extracts. Phytosomes exhibit better pharmacokinetic and pharmacodynamic profiles than conventional herbal extracts. Phytosomes are more bioavailable in comparison to simple herbal extracts. They have enhanced capacity to cross the lipid-rich biomembranes and systemic circulation. The term "Phyto" means plant while "somes" means cells-like. Therefore, the phytosomes process itself produces a little cell whereby the valuable component of the herbal extract is protected from destruction by digestive secretions and gut bacteria. Phytosomes technology has been effectively used to enhance the bioavailability of many popular herbal extracts including milk thistle, *Ginkgo Biloba*, grape seed, green tea, hawthorn, ginseng, and can be developed for various therapeutic uses or dietary supplements. These herbal extracts possess various pharmacological activities such as antimicrobial, anti-inflammatory, anti-malaria, and antiulcer among others.

Ulcers occur when the mucosal surface is broken by a lesion which extends deep down into the muscular mucosae. Gastric ulceration is a benign lesion on the mucosal epithelium upon exposure of the stomach to excess acid and aggressive pepsin activity [3]. The imbalance between these two factors, gastric acid secretion (offensive) and gastric mucosal integrity (defensive) brings about gastric ulceration [4, 5]. The mucosal wall usually defends the stomach wall and withstands the acid-pepsin attack and remains healthy but an excessive acid production or an intrinsic defect in the barrier functions of the mucosa can allow the defense mechanism to fail to lead to an ulcer. It has been reported that frequent occurrence of stress, smoking, alcohol, ingestion of non-steroidal anti-inflammatory drugs, and *Helicobacter pylori* predisposes peptic ulceration [6-8]. The incidence of complications of peptic ulcer increases with age and has been attributed to increased risk for bleeding associated with non-steroidal anti-inflammatory agents and stresses [9]. In the development of a gastric ulcer, some noxious endogenous and exogenous substances such as reactive oxygen species (ROS), primarily superoxide anions, hydroxyl radicals, and lipid peroxides, are the harmful culprits [10]. In order to mop up ROS, gastric cells have several enzymatic and non-enzymatic antioxidants such as catalase, superoxide dismutase, glutathione peroxidase, endogenous glutathione, and sulfhydryl groups, though excessive production of ROS enhances lipid peroxidation which depletes these antioxidants enzymes [11-13]. Gastric ulceration could be induced in animals using some agents such as ethanol and acetic acid [5]. The induction of gastric ulcer using ethanol causes gastric damage by altering protective factors, including decreasing mucus production and blood circulation within the mucosa [7], and by the generation of reactive species, decreased cell proliferation, and an exacerbated inflammatory response [14, 15].

The prevalence of ulcer showed that in the US, peptic ulcer disease causes an estimated 1 million hospitalization and 6500 deaths per year, while in Nigeria, the prevalence of *H. pylori* infection has been put at 70 - 90 % in adults and 82 % in children within 5 years, while globally 8 -10 % are affected of which 5 % belongs to gastric ulcer [16].

Complications of ulcer could be disastrous and life-threatening. Some of the complications include significant pain and sleeplessness, bleeding, penetration, perforation and gastric outlet obstruction among others. Based on these facts, ulcer prevention and management of ulcer are of great importance facing both production and researching Pharmacists. There had been some synthetic antiulcer drugs in existence which face a lot of setbacks such as limited efficacy and severe adverse effects. This brings about the need to divert to other agents with biodegradable, biocompatible, recyclable, non-toxic, and easily available agents. These are the herbal medications. Numerous herbal extracts have been reported to possess anti-ulcer activity. Despite this, there are several botanical products with the potential therapeutic application

because of their high efficacy and low toxicity. Some active principles in herbal extracts with antiulcer activity include flavonoids, terpenoids, and tannins. Some medicinal plant has been reported to possess antiulcers to include *Musa paradisiaca* [17], *Butea Monosperma* [18, 19], *Jatropa curcas* [20], *Mimosa pudica* [21], *Vernonia amygdalina* [22] and many others.

Musa paradisiaca is from the family of *Musaceae.* It is known as plantain which is closely related to the famous banana (*M. sapientum*). The plantain is a tall plant (3–10 meters [10–33 feet]) with a conical false "trunk" formed by the leaf sheaths of its spirally arranged leaves, which are 1.5 to 3 m long and about 0.5 m wide. The fruit, which is green, is typically larger than the common banana. Plantains are starchy fruits and are a staple food source. Medicinal values of *Musa paradisiaca* have been reported such as anti-hyperglycaemic, antiulcerogenic, antioxidant, antihypertensive, cardiac depressant, diuretic, anti-tumoral, bronchodilatory, expectorant, oral contraceptive, abortifacient, antibacterial, antifungal and among others [23]. The stem is used in the management of asthenia, wounds, and diarrhea, while the leaf has been highlighted for the treatment of inflammation, headache and rheumatism leaf [24].

In this study, *Musa paradisiaca* complexes were formulated using a novel phytosome drug delivery platform for the management of ethanol-induced gastric ulceration and the therapeutic efficiencies of the complexes investigated. Kolliphor® HS 15 was incorporated in one of the batches in order to determine if it will synergistically enhance the efficacy and bioavailability of the complexes. Kolliphor® HS 15 is a surface acting agent which reduces the surface tension of medium thereby improving the dissolution of materials. Therefore, the aim of this research was to evaluate the antiulcer activity of *Musa paradisiaca* using a modified Phytosome drug delivery.

MATERIALS AND METHODS

Materials

Methanol, petroleum ether, dichloromethane, and potassium dihydrogen phosphate (Guangdong Guanghua Sci. tech. Guangzhou, China), KCl, HCl, NaOH, distilled water (Merck, Darmstadt, Germany). Phospholipon 90 H (American Lecithin Company ALC), Kolliphor® HS 15 (BASF). Plantain (*Musa paradisiaca*) was obtained from Ogige market in Nsukka LGA of Enugu State, Nigeria.

Equipment

Magnetic heater and stirrer (SRI UM 52188, Remi Equipment, Mumbai, India), UV Spectrophotometer (T25 Basic Digital, Germany), PH meter (pH Ep, Hanna instrument, Italy), Analytical balance (Adventure, Ohaus, China), capsule (MWCO 6000-8000, spectrum labs Netherland), Filter paper (Whatman no.42, China), Wister rats (UNN Pharmacology Animal house) and Test tubes, centrifuged (SM800B, Uniscope, England).

Collection and Preparation of Plant Materials

Healthy unripe plantain fruits were obtained from Ogige market, Nsukka, Enugu state, Nigeria and the authentication was done at herbarium unit Department of Pharmacognosy, University of Nigeria, Nsukka. The peels were removed by hand cut into smaller pieces for easy drying. The dried peels were ground using a hammer mill (500♯ grinders, China). The powdered sample was packed into a screwed bottle and labeled appropriately for extraction.

Extraction and Defatting

The methanol extract of the peel was obtained by soaking 200 gram of the dried powder sample in 2.5 L of 98 % methanol for 48 h during which the mixture was intermittently shaken. It was later filtered through Whatman No 42 filter paper. The extract was concentrated by evaporation under shade for 3 days. The obtained methanol extract was added into 500 ml of petroleum ether and was shaken intermittently for 12 h at room temperature. After which the solvent was decanted and the residue was allowed to air dry under the shade. The residue was kept in an airtight container.

Determination of Percentage Yield

The percentage yield of the extract was calculated using the formula below:

$$Percentage\ yield = \frac{Weight\ of\ extract}{weight\ of\ plant\ material\ used} \times 100$$

…… Eqn1

Phytochemical Screening

Phytochemical tests of the methanol extract of *Musa paradisiaca* skin were determined using the standard methods of Trease and Evans [25].

Animal Design

The animals used in this experiment were cared for and all treatment protocols were performed in accordance with guidelines on animal ethics in

Nigeria and University of Nigeria, Nsukka which complied with European community directive for animal experiment [26]. Forty-eight healthy Wistar rats of female sexes weighing between 190-210 g were obtained from the animal unit of the Department of Veterinary Medicine, University of Nigeria, Nsukka. They were used for screening the anti-ulcer activity of the plant extract. The animals were grouped into eight groups of six animals each. The animals were kept for few weeks to acclimatize before the commencement of the experimental studies. They had free access to food and clean drinking water before the period of the experiment.

Determination of Maximum Absorbance and Preparation of Beer/Lambert's Plot

The stock solution of the plant extract was prepared by dissolving 0.1 mg in 10 ml of methanol (1mg/ml). Dilutions were performed in buffer solutions (pH, 1.2) and phosphate buffer (pH, 6.8) separately to obtain concentrations of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 µg/ml. From the concentration 8 µg/ml was selected and assayed to determine the maximum absorbance using UV/visible spectrophotometer (T25 Basic Digital, Germany). Using the lambda max, different concentrations were assayed and a plot of absorbance versus concentration was done and Beer's constant obtained.

Formulation of Phytosomes

Solvent evaporation method was employed. Complexes were prepared with a standardized extract of *Musa paradisiaca* and phospholipon 90 H at molar ratios of 1:1, 1:2 and 2:1. Appropriate weight of a standardized extract of *Musa paradisiaca* and phospholipon 90 H was dissolved in 10 ml of methanol in a 50 ml beaker using a magnetic stirrer at a temperature of about 25°C and 30°C respectively. Both solutions were mixed and 0.5 ml of Kolliphor® HS 15 was incorporated to obtain batch A (complexes with Kolliphor® HS 15), coded as AK1, AK2 and AK3 and batch B (complexes without Kolliphor® HS 15) coded as BC1, BC2 and BC3, all for molar ratios of *Musa paradisiaca:* phospholipon 90 H 1:1, 1:2 and 2:1, respectively, while the mixture was stirred for about 20 - 30 min. The resultant solutions were poured in Petri dishes and were allowed to evaporate to dryness.

Percentage Loss on Drying of the Extract

Approximately 100 mg of the extract was weighed out and recorded. It was placed in an aluminum foil and put in the oven set at 105 °C for about 1h. Thereafter, the content was reweighed until a constant weight was obtained. The percentage loss on drying was obtained using Equation 2:

$$Percentage\ loss = \frac{Original\ weight}{Weight\ after\ drying} \times 100$$

…… Eqn 2

Evaluation of *Musa Paradisiacal* Based-Phytosomal Complexes

Morphology of the Complexes

The microscopic method was used to obtain morphology of the complexes. Each of the complexes was placed on a slide by making a thin film and the film was allowed to air-dry. The morphology of the formed complex was observed using a microscope (CH 20i, Olympus) at a magnification of 4x.

Determination of Encapsulation Efficiency

Encapsulation efficiency of the complexes was determined by dissolving/dispersing accurately weighed 10 mg of each complex in 10 ml of a methanol: phosphate buffer (pH, 6.8) in a ratio 1:8 at 25 °C for 24 h. This was then centrifuged at 6000 rpm or 30 min. And the supernatant assayed using spectrophotometer at 242 nm and encapsulation efficiency was determined using Equation 3:

$$Encapsulation\ efficiency = \frac{Amount\ of\ drug\ encapsulated}{weight\ of\ the\ formulation} \times 100$$

…… Eqn 3

***In Vitro* Drug Release Study**

Approximately 10 mg of each *Musa paradisiaca* based-phytosome complexes, pure extract and standard drug were loaded in capsule and subjected to *in vitro* dissolution studies using Type-II apparatus at 50 rpm in 500 ml of simulated gastric fluid (pH, 1.2) and phosphate buffer saline (pH, 6.8) as dissolution media, maintained at 37 ± 5 °C. A 5 ml aliquot was withdrawn at 10 min intervals and the volume maintained and replaced with an equal volume of fresh medium at the same temperature. The samples were analyzed at 242 nm using UV-visible spectrophotometer (T25 Basic Digital, Germany).

***In Vivo* Studies**

The effect of *M. paradisiaca* extract on ethanol-induced gastric ulcer was investigated using the method of Mbagwu *et al.* [27]. Forty-eight rats (190-210 g) were starved for 24 h and grouped

into eight groups (AK1a, AK1b, BC1a, BC1b, EL1, EH1, PC and NC) of six each. One hour before ethanol administration, Group AK1a and b received 100 and 200 mg/kg of AK1 complex respectively; Group BC1a and b received 100 and 200 mg/kg BC1 complex respectively; Group EL1 and EH1 received 100 and 200 mg/kg of pure extract, respectively; Group PC received 50 mg/kg of Cimetidine (reference); Group NC received 2 ml/kg distilled water (placebo). All the administration was orally administered with distilled water. Then, one milliliter per kilogram weight ethanol (96 %) was then administered to all the animals to induce stress/ulcer. Four hours after ethanol administration, the animals were anesthetized with chloroform and dissected. The stomachs were excised and opened along the line of a greater curvature to expose the walls. The stomachs contents were then washed and viewed to determine the ulcer scores using the method of Raju *et al.* [28]. The ulcerative lesions were counted and scored as shown in Table 1. The percentage of ulcer inhibitions was obtained using Equation 4.

$$Percentage\ ulcer\ inhibition = \frac{UI\ (control) - UI\ (treated)}{UI\ (control)} \times 100$$

…… Eqn 4

Where, UI is ulcer index.

Table 1: Ulcerative lesions and scores

S/N	Type of ulcer	Ulcerative lesions
1	Normal stomach	0.0
2	Spot ulceration	1.0
3	Hemorrhagic streaks	1.5
4	Ulcer	2.0
5	Perforations	3.0

FTIR Spectroscopy

FTIR spectral data were taken to ascertain the structure and chemical stability of phytosome complexes, phospholipon and plant drug (*Musa paradisiacal* extract). Samples were mixed with KBr to get pellets at 600 kg/cm^2 pressure. Spectral scanning was done in the range between 4000- 400 cm^{-1} using the FTIR machine (Perkin Elmer, Spectrum BX, USA).

Statistical Analysis

Data were analyzed using SPSS Version 16.0 (SPSS Inc. Chicago, IL, US) and one-way analysis of variance (ANOVA). Values were expressed as mean ± SD (standard deviation). Differences between means were assessed by a two-tailed student's T-test and $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Percentage Yield and Loss on Drying

The yield of the extract was 60 g with a percentage yield of 60 %. The adopted method of extraction was economical and reliable to obtain such appreciable yield. The percentage loss on drying gave 17 %. This showed that the extract absorbed some moisture and therefore, should be stored in an air-tight container.

Phytochemical Tests of Methanol Extract of *Musa Paradisiaca* Peels

The phytochemical tests of the methanol *Musa paradisiaca* peel extract showed the presences of secondary metabolites such as flavonoids, glycosides, and phenols as shown in Table 2. Secondary metabolites are important to the plant as they supply nutrients to plants and provide phytochemical constituents with pharmacological activities such as antioxidant, antimicrobial, anti-inflammatory, cancer preventive, antidiabetic and antihypertensive effects [29, 30]. These phytochemical constituents have also been isolated by some previous researches [31, 32].

Table 2: Phytochemical screening of methanol *Musa paradisiaca* skin extract

Sample	Flavonoids	Glycosides	Phenols
Extract	++	+	+

Where + (present), ++ (abundantly present)

Lambda max of the *Musa paradisiacal* Extract

Musa paradisiacal extract was analyzed spectrophotometrically and the maximum absorbance of 242 nm obtained. This was used in the spectrophotometric analysis of this work.

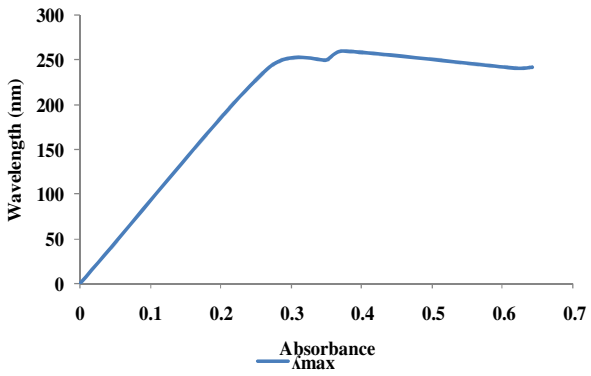

Figure 1: Plot of maximum absorbance (lambda max) of pure extract

Morphology of Different Complexes Formed

The microscopic view, as shown in Fig. 2 indicated the presence of spherical structures of the complexes. It was observed that the vesicles which consist of phosphatidylcholine 90 H and phytosomal complex intercalated well in the lipid layer. Batch A had smaller spherical vesicles than batch B. This may be due to the presence of Kolliphor® HS 15 which helped in the solubilization and reduction of particles in the complexes.

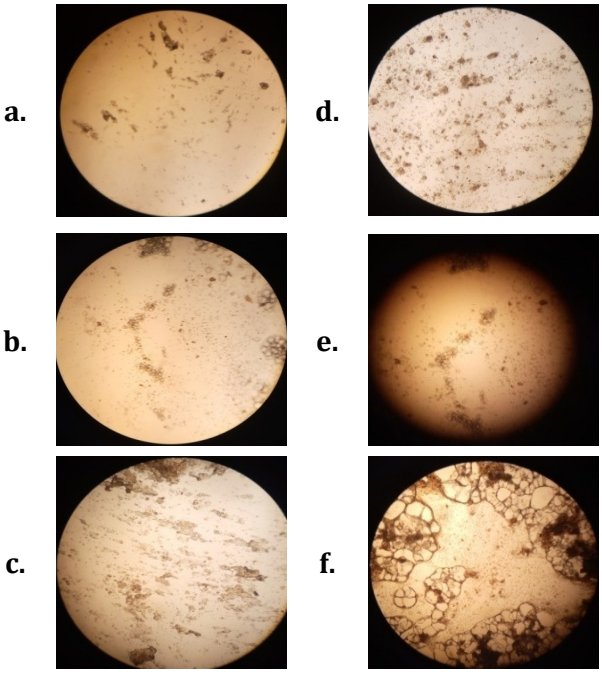

Figure 2: Morphology of *Musa paradisiacal*-based complexes

Where, a-c (AK1 – 3 i.e. batch A complexes with Kolliphor® HS 15); d-f (BC1- 3 i.e. batch B complexes with no Kolliphor® HS 15)

Encapsulation Efficiency (EE) of the *Musa paradisiacal* Complexes

Encapsulation efficiencies (EE) of the complexes are presented in Table 3. It was observed that those complexes of batch A (with Kolliphor® HS 15) significantly had the highest encapsulation efficiency ($p < 0.05$) in the range of 77.00 ± 1.30 - 93.00 ± 2.80, while the batch B was in the range of 49.00 ± 1.90 - 72.00 ± 1.60. The increasing order include AK1 > AK2 > AK3 > BC1 > BC2 >BC3. This is because Kolliphor® HS 15 enhanced the dissolution of the complexes thereby synergistically enhanced the surface area and improving the solubility of the drug with phospholipid. AK1 complex (1:1) had the highest EE ($p < 0.05$). In this respect, the optimized complex was the equal molar ratio (1:1). Therefore, a higher amount of phospholipid encapsulated the herbal extract more unlike a higher quantity of the drug.

Table 3: Drug content of the complexes

Complexes	Drug content (m±SD)
AK1	93.00± 2.80
AK2	80.00± 1.10
AK3	77.00 ± 1.30
BC1	70.00± 2.40
BC2	62.00 ± 1.60
BC3	49.00± 1.90

AK1-3 (complexes with Kolliphor® HS 15); BC1-3 (complexes without Kolliphor® HS 15).

An *In Vitro* Drug Release of the Complexes

The result of the *in vitro* drug release of the complexes as presented in Fig. 4 showed that in batch A, AK1 had a significant highest drug release ($p < 0.05$) of 85 %, while AK2 had the lowest drug release of 70 %, while in batch B, BC2 had the highest drug release of 65 %. This lower drug release of AK2 (2:1) may be due to a higher concentration of phospholipid which encapsulated more drugs within the vesicles thereby retarding the drug dissolution and release of the complex. However, the highest drug release in BC2 may be as a result of unencapsulated drugs at the periphery which increases the amount of drug present at that particular time since its EE (62 %) was not the maximum. Their T_{40} (time to release 40 % of the drug content) was 10 min for all batch A, and 20 – 30 for batch B, while their T_{60} (time to release 60 % of the drug content) were obtained at 20 – 30 min for batch A and 40 – 60 min for batch B. The significant higher time observed in obtaining 60 % of the drug content in batch B may be as a result of absent of surfactant which would have enhanced the dissolution and release of the drug. The percentage drug release of the two batches were in this order AK1 > AK3 > AK2 > BC1 > BC2 > BC3.

***In Vivo* Anti-Ulcer Activity of *Musa Paradisiacal* Complex**

The ethanol-induced gastric ulcer has been widely employed for the gastroprotective evaluation. In ethanol-induced gastric ulcer, loss of normal color and mucus along with the presence of petechiae, hemorrhage, and edema are usually observed [14]. The *in vivo* study as presented in Table 4 showed that AK1b and BC1b complex (batch A and B) at 200 mg had the higher ulcer inhibition of 85 and 55 % respectively.

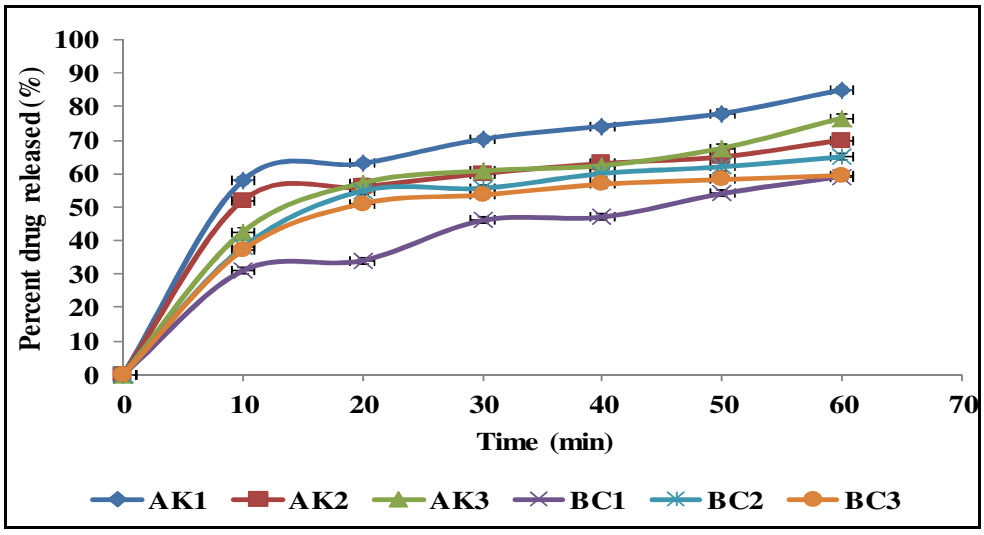

Figure 3: Graph of percentage drug release of the phytosomal complexes

The administration of high dose of *Musa paradisiaca* complex had a significant ($p < 0.05$) ulcer index and % inhibition of the ethanol-induced ulceration than others. This high dose (200 mg) of AK1b offered a better mucosal protection against ulceration than the lower dose (100 mg) which was comparable to the standard drug (PC) at 50mg/ kg. *Musa paradisiaca* extract has been found to contain some phytoconstituents which are responsible for the pharmacological activities of the plant. Among the phytoconstituents are flavonoids, glycosides and a phenolic compound which have been reported to play roles in ulcer inhibition [17, 33, 34]. Flavonoid is a phytoconstituent which had been found to increase mucosal prostaglandin content, decrease histamine secretion from mast cells through inhibition of histidine decarboxylase, inhibit *Helicobacter pylori* growth, it also serves as free radical scavengers, and finally, inhibit H^+/K^+-ATPase [35, 36]. Also, the phenol compound enhances mucus production and anti-inflammatory effect due to the presences of free radical scavenging activity. The presence of glycosides known as 'aucubin' in *Musa paradiasica* increases ulcer inhibition through its anti-histaminic activity [37]. The imbalance between aggressive factors and the maintenance of mucosal integrity through the endogenous defense mechanisms can be resolved by employing therapeutic agents which inhibit the gastric acid secretion or to boost the mucosal defense mechanisms by increasing mucosal production, stabilizing the surface epithelial cells, or interfering with the prostaglandin synthesis [38-40]. It had been reported that ulcer protection and healing effects of *Musa paradiasica* have been shown to be predominately due to its mucosal defensive mechanism together with its antioxidant activity [41]. The presences of the phytocompounds in *Musa paradiasica* augmented the mucosal protection and enhance ulcer inhibition. The batch A (AK1b) had a significantly higher ulcer inhibition ($p < 0.05$) than others and therefore, can be inferred that phytosomal complexes with an addition of surfactant-enhanced drug/extract absorption and the effect of the complex is dose-dependent.

The organs were observed to detect if there is any change in the weight due to the effect of the herbal extract of the complexes. The result of the organs weight as summarized in Table 5 showed that there was no significant change in the weight of the organ post-administration when compared to the control (NC). It can be said that this extract is safe for consumption.

Table 4: Ulcer Scores, ulcer Index and percentage inhibition of the groups

Groups	Ulcer Score (%)	Ulcer Index (cm)	% ulcer Inhibition
AK1a	40	10.00 ± 0.1	60
AK1b	35	3.75 ± 0.3	85
BC1a	50	15.00 ± 0.2	40
BC1b	45	11.55 ± 0.0	55
EL1	60	12.50 ± 0.1	50
EH1	50	15.00 ± 0.2	40
PC	45	15.00 ± 0.3	40
NC	75	25.00 ± 0.0	0

AK1a and b (low and high 1:1 complex with Kolliphor® HS 15) respectively, BC1a and b (low and high 1:1 complexes without Kolliphor® HS 15) respectively; EL 1and EH1 (low and high pure extract); PC (positive standard); NC (Negative control).

Table 5: Effect of extract on organ weight

Sample	Liver weight (mg/kg)	Kidney weight (mg/kg)
Ak1b	5.75±0.28	1.12 ± 0.03
BC1b	5.88±0.41	1.21 ± 0.03
EH1	5.59±0.55	1.04 ± 0.1
NC	6.19±0.53	1.23 ± 0.06

AK1 (a higher dose of 1:1 with Kolliphor® HS 15), BC1b (a Higher dose of 1:1 without Kolliphor® HS 15), EH1 (a higher dose of the pure extract), NC (negative control).

FTIR of *Musa paradisiacal* Complexes

The FTIR result presented in Figs. 5 - 7 showed a major characteristic absorption peaks at 1331.34, 1612.29, 1990.37, 3173.16 and 3470.28 cm^{-1} for phospholipon 90 H and 1038.1, 1458.84, 1914.32 and 2257.86 cm^{-1} for Kolliphor® HS 15 representing the presence of CN stretch, 2° amine (NH), Isothiocyanate (NCS), ammonium ion, heterocyclic amine and 1° amine, methylene, aromatic combination band, C≡C stretch, respectively. Complexes AK1 and BC1 exhibited major peaks at 1320.47, 1975.90, 2637.57, 3446.35 cm^{-1} and 1290.87, 1955.86, 2676.62, 3497.98 cm^{-1} respectively which represent aromatic amine (CN stretch), Isothiocyanate (NCS), OH stretch. The functional groups of the components were observed in the complexes. Therefore, the complexes were pure and compatible.

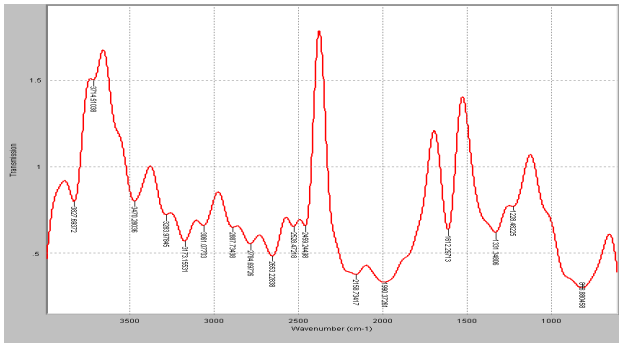

Figure 5: FTIR of Phospholipon 90 H

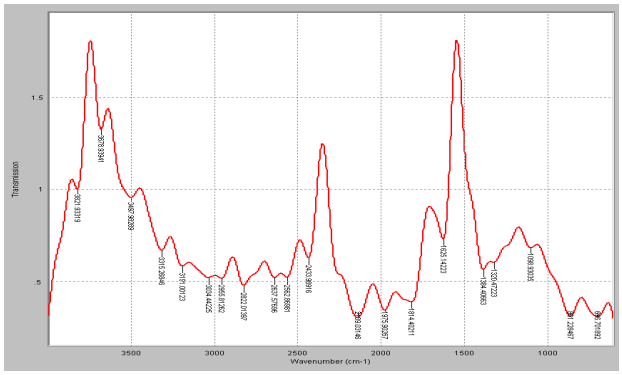

Figure 6: FTIR of AK1 (batch A)

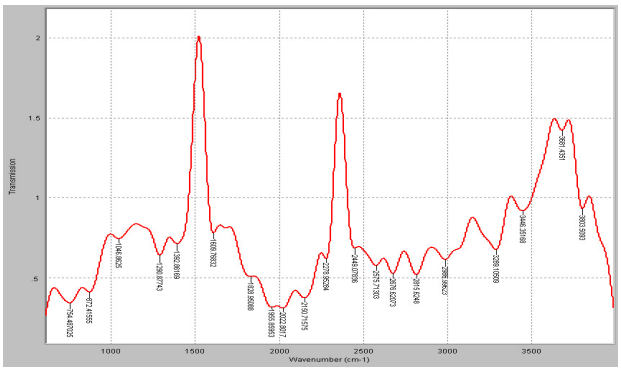

Figure 7: FTIR of CB1 (batch B)

CONCLUSION

Musa paradisiaca phytosome complexes were successfully formulated using phospholipon 90 H. The prepared phytosomes formulations were evaluated based on *in vitro* and *in vivo* antiulcer activities. FTIR confirmed that *Musa paradisiaca* and phospholipon 90H complexes were formed by non-covalent-bonds, and did not form a new compound. An agent that possesses the capacity to restore the equilibrium by enhancing the activity of the gastroprotective agents or diminishing the secretion of gastric acid could serve as an anti-ulcerative agent. Batch A complexes had higher activity due to synergistic activity of Kolliphor® HS 15 than others. Therefore, phytosomes is a promising approach for the delivery of herbal medicine. A higher dose of the complex inhibited ulcer formation comparable to the standard (Cimetidine). Musa paradisiaca complex was observed to ameliorate ethanol-induced gastric ulceration which may be attributed to antioxidative and mucus defensive mechanism. Presence of phytochemicals contributed to the antiulcerogenic activity. Therefore, the methanol extract of *Musa paradisiaca* peel mimicked the action of a standard anti-ulcer drug by ameliorating ulcers in the experimental model adopted.

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