Full Length Research Paper

Preparation, characterization, *in vitro* and *in vivo* evaluation of PEGylated-mucin matrix tablets containing aqueous leaf extract of *Vernonia amygdalina*

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The objectives of this research were to formulate and evaluate PEGylated mucin matrix tablets containing *Vernonia amygdalina* leaf water extract. PEGylated mucin matrices formulated with PEG 8000 and mucin from the African land snail *Archachatina marginata* at ratios 1:1, 0:1, 1:0, 3:1 and 1:3 were used to prepare *V. amygdalina* tablets by dry granulation and direct compression. Characterization based on surface morphology, weight uniformity, friability, hardness/crushing strength and absolute drug content were carried out on the tablets. The *in vitro* release studies were performed in phosphate buffer saline (PBS, pH 7.4), while the *in vivo* release studies were conducted using alloxan-induced diabetic rats. The results obtained showed that the tablets were smooth and circular in shape, maintained a percentage deviation of 3 to 5% in the weight uniformity test, had percentage average resistances (friability) less than 1% and crushing strengths less than 5 kgf, and thus conformed to compendial requirements for acceptance. *In vitro* release studies indicated sustained release potentials of the tablet formulations. Further kinetic analysis of drug release showed predominance of the Higuchi square root model and Fickian diffusion release mechanism. *In vivo* antidiabetic study revealed mucin-dependent glucose lowering potentials of the tablets which were significantly ($p < 0.05$) greater than those of commercial glibenclamide tablets. The method of prepartion of PEGylated mucin tablets needs to be carefully selected to ensure the production of tablets with adequate bond strength to withstand the rigours of handling and at the same time release the active compound(s) for biological action.

Key words: *Vernonia amygdalina,* PEGylated-mucin, hyperglycaemic, tablet.

INTRODUCTION

Type II diabetes is a debilitating disease that arises from improper energy storage and utilization. The global pre-valence of type II diabetes, which is presently estimated to affect more than 100 million people, is set to double by the year 2010. Statistical and epidemiological data clearly show increasing prevalence of diabetes with time (Manna

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time (Manna et al., 2004; Lefebuvre, 2005). Hence, there is an urgent need to synthesize more effective and oral antidiabetic agents.

The emergence of drug resistance is reducing the therapeutic arsenal for the treatment of diabetes cases at a rate that is barely balanced by the development of novel effective drugs. In this regard, medicinal plant research has become more important particularly after looking into the history on medicinal plants used by the traditional healers (Momoh and Muhamed, 2011; Uchenna et al., 2008). Natural plant products are main sources of biologically active compounds and have potential for the development of novel anti-diabetes drug. Traditionally, plant medicines are used throughout the world for a range of diabetic presentations. Therefore, an investigation of such agents from traditional medicinal plants has become particularly important. Many countries in Africa have a rich history of using various potent herbs and herbal components for treating diabetes and many other diseases. Many plants have previously been investigated for their beneficial use in different types of diabetes (Ebong et al., 2006). Among these plants, *Vernonia amygdalina* has been widely researched in the area of diabetes management (Ebong et al., 2006).

Polyethylene glycol (PEG) is a nontoxic and non irritant hydrophilic polymer (Zabaleta et al., 2007) that is used in PEGylation either with other polymer or alone in the delivery of drug molecules (Murugesan et al., 2008). PEGylation of proteins, drugs, liposomes and nano-particles has been proven to be an effective approach for extending circulation in the blood stream, owing to the steric hindrance of the PEG chains (Momoh and Adikwu, 2008). Mucins are high molecular weight glycosylated proteins, believed to be the major structure-forming component of mucus (Adikwu and Ndu, 2006) and responsible for the cohesive and visco-elastic nature of mucus gel (Momoh et al., 2010). Pure mucin is the glycoprotein part of the mucus devoid of water, free proteins, minerals and lipids (Adikwu et al., 2005). Apart from acting as protectants and lubricants, mucins are known to be the substrate on which mucoadhesive polymers attach, thus the interest in hybridizing them with other polymers (Builders et al., 2008).

From this previous knowledge, this work was aimed at designing PEGylated-matrix tablet based on PEG:mucin blends for used as novel carriers for the delivery of *V. amygdalina* extract.

MATERIALS AND METHODS

The following materials were purchased from their local suppliers and used without further purification: Polyethylene glycol-8000 and alloxan monohydrate (Sigma St. Lious, USA), citric acid, sodium hydroxide (Merck, Germany), paraldehyde injection (Kamala India), methyl red, ethanol, nitric acid, silver nitrate, tetraoxosulphate (vɪ) acid, sodium chloride, acetone, concentrated HCl (BDH, England).

Phosphate buffer pH (7.4) was prepared following the compendium (USP XXIII) specification. All other reagents were of analytical grade and were used as such.

Animals

Albino rats

Mature Wistar albino rats weighing between 95 to 130 g obtained from the Department of Biochemistry, University of Nigeria, Nsukka and fed on 'chicks marsh`` (Top Feed, Nigeria) were used for the study. All the rats were allowed to equilibrate in standard and conditioned animal houses at the Department of Biochemistry, University of Nigeria for a period of one week before use.

Extraction of snail mucin (slime)

The giant African land snails (*Archachatina marginata*) used was procured from a local market in Nsukka, Enugu State. The method described by Adikwu and Nnanami (2005) was employed in the extraction of snail mucin.

Extraction of *V. amygdalina* leaf constituents

The fresh leaves of *V. amygdalina* plant were collected from Nsukka, Enugu State, Nigeria and identified at Bioresources Development and Conservation Program (BDCP), Nsukka. The clean leaves were sorted, washed without squeezing and sun-dried for seven days. The dried leaves were milled into coarse powder using an End runner mill. A 1.0 kg quantity of the resulting powder was soaked in three litres of distilled water, shaken and allowed to stand for 48 h. The resulting mixture was filtered through a Whatman No. 1 filter paper and concentrated by drying at 40°C in an oven to obtain the crude aqueous extract (8.5 g) which was then stored in an air tight container until used.

Preparation of unloaded PEGylated-mucin matrices

Unloaded PEGylated-mucin matrices were prepared by solvent evaporation method. Briefly, 5 g of PEG and mucin were dissolved separately in 30 ml of highly purified water with a magnetic stirring set up (300 rpm) in a 100 ml beaker until a uniformly dispersed system was obtained. After 4 h, the mucin mix was then dispersed in the PEG solution using magnetic stirring (300 rpm) and allowed to stand undisturbed for 24 h. A 500 ml volume of chilled acetone maintained at -30°C was then slowly added into 250 ml beaker containing the pegylate with constant stirring at a speed of 100 rpm, for 30 min, in an ice to regulate the temperature (owing to the nature of mucin). The PEGylated-mucin samples formed were collected by filtration through a milliport filter 0.22 µm. Detail of the ratios used in the preparation of unloaded PEGylated mucin matices are shown in Table 1.

Physical properties of PEGylated mucin matrices

The micrometric properties of microparticles such as; bulk and tapped densities and angle of repose were determined. The compressibility indices of the particles were also evaluated from the bulk and tapped density using Equations 1 to 4.

Table 1. Ratios of mucin and PEG used for preparing unloaded microparticles.

Batch code	PEG	Mucin
A	1	1
B	0	1
C	1	0
D	3	1
E	1	3

$$\text{Bulk density} = \frac{\text{Mass of Powder (M)}}{\text{Bulk volume of powder } (V_B)} \quad (1)$$

$$\text{Tapped density} = \frac{\text{Mass of sample (M)}}{\text{Tapped volume } (V_T)} \quad (2)$$

$$\Theta = \tan^{-1} h/r \quad (3)$$

$$\text{Carr's Index (\%)} = \frac{\text{Tapped density – Bulk density}}{\text{Tapped density}} \times 100 \quad (4)$$

Morphology and particle size analysis

Particle size analysis was carried out on the microparticles using a digital light microscope (Leica Diestar, Germany) and images captured with Moticam 1000 camera. The morphology and sizes of the particles were determined based on image analysis of the microparticles.

Preparation of PEGylated mucin tablets

PEGylated-mucin tablets containing 200 mg equivalent to (300 mg of tablet) *V. amygdalina* (VA) extract were prepared, according to the formula shown in Table 1 by direct compression. The various component, namely PEGylated-mucin matrices, *V. amygdalina* (active pharmaceutical ingredient), lactose and microcrystalline cellulose (bulking agents) were passed through a sieve no. 20, separately. Mixing of powders was done manually using a pestle and mortar for 5 min. Starch (binder) and magnesium stearate (external lubrication) were then added to the mixed powders, it was further mixed for another 5 min. A 300 mg of each mixture were weighed and fed manually into the die of a single punch tabletting machine (F3 Manesty, England) equipped with flat-faced punches 9.0 mm, to produce the desired tablets at a compressed force of 48 kgf.

Characterization of PEGylated mucin tablets

Absolute drug content

Twenty tablets were selected randomly from each batch, weighed together and crushed in a mortar with a pestle. An amount equivalent to the average weight of the crushed tablets was weighed, dispersed in phosphate buffer (pH 7.4) and heated for 30 min. The dispersion was allowed to cool, filtered and an aliquot of the resultant filtrate was analysed for content of *V. amygdalina* leaf extract spectrophotometrically (Unico UV 2102 PC Spectrophotometer, USA) at 254 nm, which was repeated three times for each batch. This was used to calculate the absolute drug content in each batch with reference to standard Beer's plots for *V. amygdalina* leaf water extract in phosphate buffer.

Tablet weight uniformity

Twenty tablets from each batch were weighed together and individually and the mean weight and percentage deviation calculated according to British Pharmacopoeia (2009).

Tablet thickness

A vernier caliper (For-bro Engineers, Mumbai, India) was used to determine thickness of 10 randomly selected tablets. Results are expressed as mean values ± standard deviation (SD).

Tablet friability

According to the BP specifications (Howard, 2006), ten tablets were randomly selected and placed in the drum of a tablet friability test apparatus (FAB-2, Logan Instruments Corp., NJ, USA). The drum was adjusted to rotate 50 times in 5 min. The tablets were removed, de-dusted and accurately weighed. The percent weight loss was calculated.

In vitro release studies

The release rate of the VA tablet was studied. The release rate studies were carried out in 900 ml of phosphate buffer (pH 7.4) using USPXXIII dissolution apparatus (Electrolab) with a pedal stirrer, according to United States pharmacopoeia (USP). The tablet equivalent to 200 mg of VA was used in each test. The stirrer was adjusted at 100 rpm, and the temperature was maintained at 37 ^{0}C ± 0.5 ^{0}C throughout the experiment. A 2 ml sample was withdrawn at various time intervals, filtered, and the filtrate was analyzed for drug release at 254 nm after suitable dilution with phosphate buffer. All the release experiments were conducted in triplicate (n=3).

Kinetic analysis of in vitro release profiles

In order to understand the mechanism and kinetics of release of *V. amygdalina* leaf extract from the PEGylated mucin tablets, the results of the *in vitro* drug release study were fitted into various kinetic equations like zero order (Cumulative percent drug released vs. Time), first order (Log cumulative percent drug retained vs. Time), Higuchi (cumulative percent released vs. √T), Peppas (Log of cumulative percent drug released vs. log Time) and Hixson-Crowell's cube root model ((Percentage retained) $^{1/3}$ vs.Time) as depicted in Table 5. The kinetic model that best fits the dissolution data was evaluated by comparing the regression coefficient (r) values obtained in various models. In the Peppas (Fickian diffusion) model, mechanisms of drug release are characterized using the release exponent ('n' value). An 'n' value of 1 corresponds to zero-order release kinetics (case-II transport); $0.5 < n < 1$ means an anomalous (non-Fickian) diffusion release model; $n = 0.5$ indicates Fickian diffusion and $n > 1$ indicates a super case-II transport relaxational release (Ofokansi et al., 2007).

Table 2. Different treatment used for *in vivo* evaluation.

Group	Treatment
1	Batch A (1:1)+200 mg of VA
2	Batch B (0:1)+200 mg of VA
3	Batch C (1:0)+200 mg of VA
4	Batch D (3:1)+200 mg of VA
5	Batch E (1:3)+200 mg of VA
6	Batch F Glibenclamide only
7	Batch G Distilled water

A = 1:1 of PEG :Mucin, B = 0:1 of PEG :Mucin, C = 1:0 of PEG :Mucin, D = 3:1 of PEG :Mucin, E = 1:3 of PEG :Mucin; Each batch contains 200 mg of *V. amygdalina.*

In vivo studies in rats

The *in* vivo efficacy of VA tablet was carried out in alloxan monohydrate induced diabetic rats. The animal experiments were carried out in accordance with the guidelines and protocol approved by the Animal Ethics Committee, Department of Pharmaceutics, University of Nigeria Nsukka. Wistar rats of either sex weighing between 180 to 200 g were fasted for 18 h prior to the study. Alloxan monohydrate dissolved in normal saline as a vehicle at a dose of 200 mg/kg body weight was administered intra-peritoneal to render animals diabetic. Blood glucose levels were monitored daily for 7 days for all the rats until the induction and stabilization of diabetic state. Diabetic animals were divided into 7 groups of 5 animals each and were administered orally with various batches of the prepared tablet according to body weight of the animal (Table 2). Blood samples were taken from the tail at predetermined time intervals and examined for the glucose concentration using glucometer (Accu-chek[®], Roche, Switzerland). The post-dose levels of the blood glucose were expressed as a percentage of the predose level. The percent basal blood glucose concentration was plotted against time for the various groups.

$$\% \text{ Glycaemic change} = \frac{Initial\ Conc - Final\ Conc}{Initial\ Conc} \times 100$$

Statistical analysis

The data represented as mean ± standard error of mean (SEM). Statistical significance between the treated and control groups was analyzed by means of students' 't'-test. For group comparisons, the one-way layout analysis of variance (ANOVA) with duplication was applied and the significant differences in the mean values were evaluated. Values ≤ 0.05 were considered statistically significant.

RESULTS AND DISCUSSIONS

The bulk and tapped densities as well as the angle of repose of the granules are shown in Table 3. The bulk and tapped densities of the granules were within the range of the intended material for tablet preparation. The particle shape (pictures not shown) and sizes range from 189 to 245 μm, the shape of PEGylated-mucin microparticles

are less spherical than the microparticles prepared by either of the polymer.

Tablets evaluation

The tablets prepared with PEGylated-mucin matrix exhibited good friability results comparable to the tablets prepared with the individual polymer. Values of friability (B) up to 0.8 to 1% are quoted as upper level of acceptance (Chukwu et al., 1997). From Table 4, all the batches of the tablets formulated complied with BP standards for friability test. The disintegration time of all the tablets were within the accepted range (Chukwu et al., 1997), the disintegration time of PEGylated for-mulation is slightly higher than the tablet formulated with individual polymer. However, batch E tablet prepared with (1:3) PEG: mucin ratio showed the highest disintegration time of 20.8 min. This effect may be associated with the polymer ability to absorb water forming gel, thereby delaying the burst effect of tablet. The absolute drug contents of the PEGylated mucin tablets are represented as a bar chart in Figure 1. The figure shows that all the tablet batches showed good loading efficiency. However, the loading efficiency of *Vernonia amygdalina* in the tablets in increasing order was as follows: batch C < batch D < batch B < batch A < batch E. By implication, PEGylation of mucin created numerous spaces for drug localization, which was effectively achieved with higher concentration of mucin than PEG 8000. In other words, the drug contents were dependent on the composition of the PEGylated mucin tablets. The higher values of the encapsulation efficiency observed may be due to increase in core material in the tablets. Batch E containing three parts of mucin and one part of PEG 8000 entrapped the greatest amount of *V. amygdalina* leaf water extract in the tablets in comparison with the other batches (A to D). The drug entrapment efficiency is an important variable for assessing the drug loading capacity of tablets and their drug release profiles, thus suggesting the amount of the drug that would be available at the absorption site. This parameter is dependent on the preparation method, physicochemical properties of the drug, and the formulation variables (Umeyor et al., 2011).

In vitro drug release form the tablets

The release of *V. amygdalina* from PEGylated tablets varied according to the proportion of matrix forming polymers employed in the study. Ideally, a sustained release tablet should release the required quantity of drug in order to maintain an effective drug plasma concentration. From *in vitro* drug dissolution profile of PEGylated tablet (Figure 2), it was found that batch E

Table 3. Micromeritic properties of *V. amygdalina* loaded PEG-mucin matrices.

Batch code/ PEG:Mucin	ℓ_B (g/ml)*	ℓ_T (g/ml)*	A.R (^{o})*	HR	PS µm
A (1:1)	0.49±0.01	0.59±0.003	21.1±0.21	1.01	243
B (0:1)	0. 53±0.05	0.57±0.006	24.5±0.20	1.02	245
C (1:0)	0.51±0.01	0.69±0.010	28.2±0.35	1.04	188
D (3:1)	0.46±0.010	0.61±0.010	26.5±0.13	1.02	172
E (1:3)	0.52±0.01	0.63±0.005	26.1±0.27	1.05	177

A = 1:1 of PEG :Mucin, B = 0:1 of PEG :Mucin, C = 1:0 of PEG :Mucin, D = 3:1 of PEG :Mucin, E = 1:3 of PEG :Mucin; Each batch contains 200 mg of *V. amygdalina*. Values shown are mean ± SD (*n = 3); ℓ_B and ℓ_T = Bulk and tapped densities, AR = Angle of repose, HR = Hausner's ratio, PS= particles sizes.

Table 4. Physical properties of the PEGylated mucin tablets.

Batch/ Tablet code	Weight (mg ± CV)	Hardness (KgF)	Friability (%)	Disintegration time (min)
A (1:1)	303.3±1.80	4.90±0.20	0.10	17.0±0.10
B (0:1)	3001.0±1.66	5.11±0.20	0.40	14.4±0.21
C (1:0)	304.1±0.48	4.96±0.08	0.30	12.8±0.12
D (3:1)	303.5±2.39	4.96±0.08	0.10	16.1±0.11
E (1:3)	306.2±1.15	4.89±0.20	0.00	20.8±0.12

A = 1:1 of PEG :Mucin, B = 0:1 of PEG :Mucin, C = 1:0 of PEG :Mucin, D = 3:1 of PEG :Mucin, E = 1:3 of PEG :Mucin; Each batch contains 200 mg of *V amygdalina.*

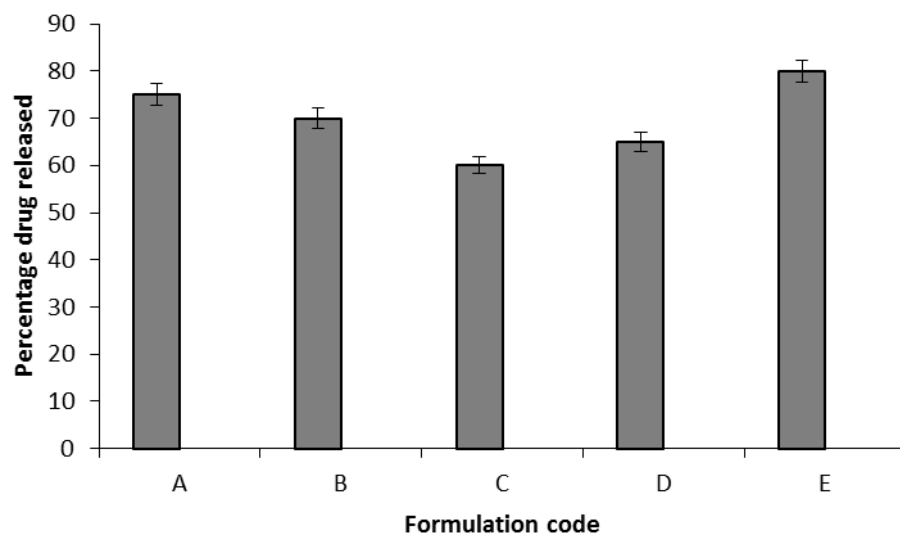**Table 5.** Kinetics of release of *V amygdalina* leaf extract from the PEGylated mucin tablets.

Formulation Code	Zero-order (r^2)	First-order (r^2)	Higuchi (r^2)	Hixson-Crowell (r^2)	Ritger-Peppas parameters		
					r^2	K	n
A	0.8406	0.9197	0.9280	0.8688	0.9787	0.8490	0.61
B	0.9813	0.9328	0.9095	0.9375	0.9186	0.9791	0.59
C	0.8430	0.9895	0.9352	0.9940	0.9362	1.1716	0.49
D	0.9221	0.9641	0.9284	0.9877	0.9776	1.3448	0.45
E	0.9208	0.8916	0.9467	0.8156	0.9675	1.2436	0.46

A = 1:1 of PEG :Mucin, B = 0:1 of PEG :Mucin, C = 1:0 of PEG :Mucin, D = 3:1 of PEG :Mucin, E = 1:3 of PEG :Mucin; Each batch contains 200 mg of *V amygdalina.* n = Release exponent; k = Release kinetic constant; r^2 = Square of correlation coefficient.

provided highest release, followed by batch D and A. The high amount of VA release from batch E could be attributed to polymer ratio. The interaction of the PEG-mucin creates a bond within the content of the formulation and create inter pressure within, this led to high water absorption. This water uptake leads to the considerable swelling of the polymers and create an opening in the tablets thereby causing the drug to diffuse from the tablets at a faster rate. Batches B and C prepared with individual polymers released lesser amount of VA in comparison with batches A, D and E. The PEG being a hydrophilic polymer (Zabaleta et al., 2007; Momoh et al., 2010; Murugesal et al., 2008) solvated in the medium and gave early drug release (bulk effect) within a short time, however, mucin having a soluble and non-soluble component (Ofokansi et al., 2007; Adikwu and Nnamani, 2005; Builders et al., 2008; Momoh and Adikwu, 2008) showed a different scenario. It could be possible that the gel nature of mucin (Builders et al., 2008) hindered the diffusion of the drug to the surface, hence the poor release of VA from the tablets.

The release behavior of VA from batches containing

Figure 1. Percentage content of *V amygdalina* leaf water extract in the PEGylated mucin tablets. A = 1:1 of PEG :Mucin, B = 0:1 of PEG :Mucin, C = 1:0 of PEG :Mucin, D = 3:1 of PEG :Mucin, E = 1:3 of PEG :Mucin; Each batch contains 200 mg of *V amygdalina*
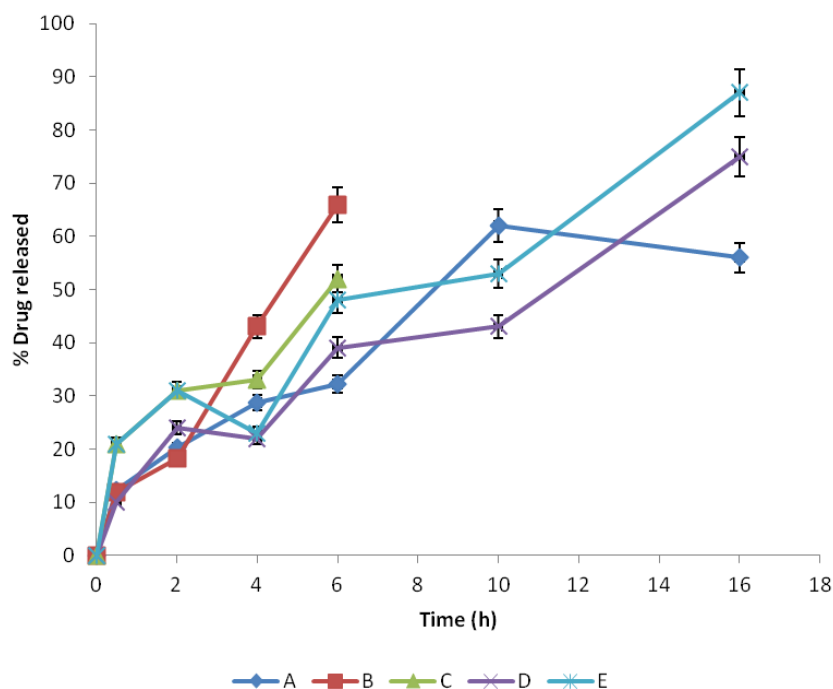
Figure 2. The release of *Vernonia amygdalina* from the tablets. A = 1:1 of PEG :Mucin, B = 0:1 of PEG :Mucin, C = 1:0 of PEG :Mucin, D = 3:1 of PEG :Mucin, E = 1:3 of PEG :Mucin; Each batch contains 200 mg of *V amygdalina*

PEG and mucin at the ratio of 3:1 (D) and 1:3 (E), respectively were very impressive, since both formulations showed effective controlled release pattern, although, the formulations showed a $T_{50\%}$ within 6 h, while batches A, D and E maintained further release up to 80% for a period the study lasted. This effect could be due to the contribution of the polymers. PEG being a hydrophilic polymer has the tendency to absorb water easily (Zabaleta

et al., 2007; Momoh et al., 2010; Murugesal et al., 2008), hence the faster release within the first 30 min to an hour in all the formulations. In addition, mucin being a biological substance with two phases (soluble and insoluble part) (Ofokansi et al., 2007; Adikwu and Nnamani, 2005; Builders et al., 2008; Momoh and Adikwu, 2008), the tablets swelling behavior occurs because of the formation of inter-polymer complexes between functional groups and the steric groups on the PEG chains. This inter-polymer complexation is a thermodynamically favorable event, which is an added advantage to prolong released of VA in this study.

In vitro release kinetics and mechanisms

Different mathematical models were used to describe the kinetics of release of *V. amygdalina* leaf water extract from the PEGylated mucin tablets. The criterion for selecting the most appropriate model was chosen on the basis of goodness-of-fit test. The result is presented in Table 5. A comparative evaluation of the (r^2) values for the tablets shows that all the formulae exhibited the highest regression coefficient when the percentage of the drug released was plotted against the square root of time. These data revealed that the PEGylated mucin tablets obeyed both the Ritger-Peppas and Higuchi membrane diffusion-controlled models better than other models and thus exhibited diffusion-controlled release characteristics. In other words, the release data indicated that the Ritger-Peppas and Higuchi square root models were the predominant models of drug release from the PEGylated mucin matrix; all the batches of tablets obeyed the Ritger-Peppas and Higuchi square root models. With respect to the (Ritger-Peppas) Fickian diffusion model, the values of the release rate constant, k, and the release exponent, n, indicate that the release of *V. amygdalina* leaf water extract from the PEGylated mucin tablets in phosphate buffer predominantly occurs by diffusion following non-Fickian transport mechanism (James et al., 1997; Ofokansi et al., 2007).
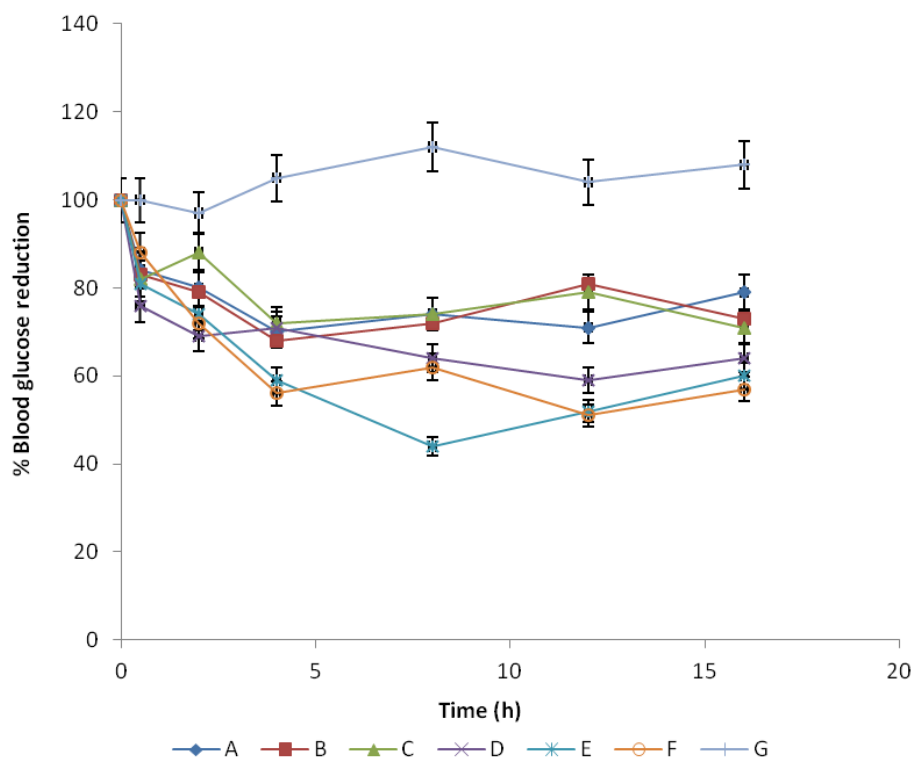
Glucose reduction level

The effectiveness of the VA tablet prepared with PEGylated-mucin matrices was assessed based on its capabilities to reduce blood glucose level in an alloxan induced diabetic rats (Uchenna et al., 2008). The orally administered pure glibenclamide dispersed in water and the distilled water in groups F and G, respectively, serve as controls. The doses used in this study were administered according to the animal weight. The percentage reduction of initial glucose level was used as an evidence of the amount of *V. amygdalina* released and absorbed into the systemic circulation (Uchenna et al., 2008; Ebong

et al., 2006), hence the reduction. Figure 3 shows the various blood glucose reductions obtained from the study, the percent blood glucose reduction from initial glucose levels versus time were plotted. The mean blood glucose baseline (initial glucose level) value was taken as the 100% level and others were based on the initial basal blood glucose level. The rats that received distilled water (group G) continued to have elevated blood glucose levels throughout the period of study. The positive control group, glibenclamide (F) showed an initial blood glucose reduction with an early burst effect within 2 h, the effect was sustained up till 12 h, the percentage reduction was slightly less than the formulated tablet at 8 h and this was significant (p < 0.005) enough to prove that the commercial sample was not better than the prepared *V. amygdalina* tablet (batch E).

The VA-loaded PEGylated mucin tablets (batch A, D and E) reduced the glucose levels of the rats higher as compared to when the polymers were used alone (batch B and C), consistent with a previous study (Momoh et al., 2011). In other words, the combined polymers showed better glucose lowering effect than other formulations throughout the 12 h of study. Highest blood glucose lowering (56%) was encountered in the (batch E). The tablet with high mucin content (batch E) showed a steady and prolonged antidiabetic effect, and this was relatively higher than the blood glucose reduction (49%) encountered in the conventional tablet sample of glibenclamide at 8 h. Formulations A, D E prolonged the drug effect for 16 h (Figure 3). The prolong effect observed in A, D and E may not be unconnected with the polymers used. This shows that *V. amygdalina* formulated could effectively be delivered as tablet using PEGylated matrix. It further suggests that the release of VA from the tablet stimulated the production of insulin from islet cells of Langerhans in a much more controlled manner than the conventional tablet form.

Studies have shown that, incorporating mucoadhesive properties into a drug-delivery system has many significant advantages compared to traditional pharmaceutical dosage forms (Builders et al., 2008; Adikwu and Nnamani, 2005; Sharma et al., 2006). The mucoadhesive properties can maintain the drug-delivery system in a specific location in the body, have a prolonged duration of contact with the tissue, and increase the treatment efficiency since the drug is locally maintained at the site of transport. This is important since localizing the drug at a targeted site of absorption and transporting the drug across the intestinal epithelial layer are two problems associated with the low bioavailability that often plagues oral drug delivery (Umeyor et al., 2011). Increased contact of the drug-delivery system with the mucosal absorptive membranes for an extended period could increase the absorption of the therapeutic agent, resulting in a higher drug bioavailability, and this was one of the primary functions of mucin in our formulations (Builders

Figure 3. Percentage reduction in blood glucose level in diabetes rats treated with oral tablet of *V* amygdalina. A = 1:1 of PEG :Mucin, B = 0:1 of PEG :Mucin, C = 1:0 of PEG: Mucin, D = 3:1 of PEG :Mucin, E = 1:3 of PEG :Mucin; Each batch contains 200 mg of *V. amygdalina.*

et al., 2008; Adikwu and Nnamani, 2005; Sharma et al., 2006).

Conclusion

The results obtained from our studies showed the effectiveness of the PEGylated-mucin as a novel carrier system for oral delivery of VA as tablet dosage form. The samples prepared with (1:3) of PEG and mucin produced blood glucose lowering effect which was relatively higher than the conventional glibenclamide 8 h after oral administration. This indicates that conventional delivery of *V. amygdalina* for effective control of blood glucose is indeed possible using the right carrier system and formulation technique. We have also demonstrated the safety of VA in our previous research (Momoh et al., 2011).

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