RESEARCH PAPER

Model Drug Loaded Loaded Bio-Nanoparticular Dispersion Utilizing a Novel Biomaterial Isolated from Natural Flower Petals: Development, Evaluation and Elucidation of Drug Release Kinetics and Mechanisms

Dr Sushant Kumar[1], Dr Swarnima Pandey[*2], Dr Neha Jaiswal[3], Nusiba Albasheer[4], Mehrukh Zehravi[5], Pragya Chaudhary[6]

[1]Faculty of Pharmacy, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, 206130, U.P.

[2]Department of Pharmacy, Apex college of Pharmacy, Rampur, Uttar Pradesh

[3]Department of Pharmaceutics, College of Dentistry and Pharmacy, Buraydah Private Colleges, Buraydah, Al-Qassim, Saudi Arabia

[4]Department of Pharmaceutical Analysis, Sudan International University

[5]College of Dentistry and Pharmacy, Buraydah Private colleges, Buraydah, Saudi Arabia

[6]School of Pharmacy, Dev Bhoomi Uttarakhand University, Dehradun, UK

Corresponding author: *Dr Swarnima Pandey - yesgoldi@gmail.com

ABSTRACT

In an endeavor to ameliorate the protracted fiscal burdens associated with epilepsy management and to increase therapeutic efficacy, this investigation harnessed an innovative bio-material extracted from Cestrum nocturnum flower petals to formulate a phenytoin-loaded bio-nanoparticular dispersion. The development of a nanocapsulated dispersion system necessitated the isolation of a novel biomaterial endowed with exceptional intrinsic attributes. This biomaterial was combined with the phenytoin as an antiepileptic agent in varying ratios (1:2, 1:4, 1:6, 1:8, 1:10) to fabricate formulations NSPHNP1 through NSPHNP5. Comprehensive assessments of yield, stability, pH, entrapment efficiency, dispersibility, zeta particle size, In-vitro-drug release were conducted on the bio-nanodispersion. Spectrophotometric analyses corroborated that the isolated biomaterial exhibited properties commensurate with standard polymers. The NSPHNP5 formulation demonstrated superlative performance across multiple evaluation parameters, achieving an entrapment efficiency of 92.47 ± 1.02%, a pH of 7.4 ± 0.01, t50-17.26hr, t80-31.16hr, r^2 0.9899 and exemplary nanoparticle dispersibility. The bio-nanodispersion, formulated with a biomaterial possessing remarkable stabilizing and retardant properties, proved to be both safe and stable for encapsulating the nanosized model drug phenytoin, thereby offering a promising platform for advanced drug delivery systems.

Keywords: Natural petals, biomaterial, biopolymer, nanosizing, bio-nanodispersion, nanoparticles

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INTRODUCTION

Polymeric materials are a crucial foundation in responding to the multi-faceted character of problems encountered in next-generation drug delivery systems development. The macromolecules have temporally controlled and sustained delivery of drugs, with hydrophilic and lipophilic polymers being especially well-suited to enable sustained, extended, or targeted delivery to specific body locations. These modalities are very dissimilar to the traditional chemical processing methods used in the manufacture of semisynthetic and synthetic polymers, which have been shown to exhibit high economic burdens and incompatibility problems, leading scientists to seek bio-compatible and eco-friendly modalities[1].

Nature-derived biomaterials are a new trend in nanostructured drug development, and it is a solution for synthetic and semisynthetic polymers in a sustainable way[2,3].

These polymers derived from nature are unmatched in their creativity and flexibility, having been purified from a wide variety of ordinary sources. In the delivery of drugs across the central nervous system, nanoparticles have proven to be an unparalleled delivery carrier, ascribable to their diminutive size, nano-range size which facilitates an easy crossing across the BBB and selective targeting within cerebral tissue[4]. Nanoparticles developed from novel biomaterials, known as bio-nanodispersions, are biocompatible and biodegradable and thus well-suited to administer the antiepileptic drug phenytoin in a controlled manner to treat the disease effectively[5].

Epilepsy is a neurological disease with disturbed cerebral electrical activity in uncontrolled manner that appears as recurrent, uncontrollable fits or seizures. The paroxysmal attack initiates due to disturbances in the electrophysiological balance of the brain, which are induced by multifarious etiologic elements. The current study uses a newly synthesized seed-derived biomaterial of Cestrum nocturnum for the formulation of a phenytoin-loaded bio-nanodispersion, which is an efficient substitute for traditional polymers. This biomaterial, both intrinsically biocompatible and biodegradable in character, holds the promise to be a groundbreaking excipient in pharmaceutical nanotechnology[6].

MATERIALS AND METHODS

Materials

Phenytoin is a type of drug whose model was gratefully provided by Affy Pharma Private Limited, Baddi. Seeds of Cestrum nocturnum were purchased in the commercial local market of Lucknow, India. All the other chemicals that were used were of analytical grade and methods modern.

Methods

Separation of biopolymers through a low cost and eco-friendly process extremely streamlined techniques were used in isolating biomaterial. The flower petals of Cestrum nocturnum were washed with distilled water then 100 mL of water was added, filtered through muslin cloth to yield a crude filtrate of the flower petals. The above filtrate was subsequently centrifuged (5000 rpm, 20 minutes) and the supernatant mixed with methanol in the proportions of 1:2 and stored at a refrigerator overnight. The centrifugation of precipitate was done at 5000 rpm duration of 30 minutes and the remnant containing the biopolymer was dried under vacuum. This residue was further washed using chloroform and acetone to ensure that all the impurities are eliminated. It was dried to give free-flowing powder, sieved through a 120-mesh sieve, and stored in air tight containers.The process was repeated six times to achieve the maximum yield, relative to the original crude material in terms of percentage dry biomaterial[7].

Yield of bio-material

The consultations were made through six separate determinations on a digital scale in percentage of the dry biomaterial weight against the initial crude material weight and computed standard deviations in the view of delivering statistical stability[7].

Physico-chemical testing of biomaterial

Physical properties of the biomaterial were well assessed like color, smell and texture. Its color change temperature was also obtained using the assistance of melting point instruments, whereby the biomaterial has been placed into a capillary tube and starts heating until a noticeable alteration in color and melting takes place [8].

Analysis of chemical constituent

Analysis of carbohydrate

A solution of 5% biomaterial (1 mL) was placed in a test tube then 2 drops of Molisch reagent placed in the test tube followed with 1-2 mL of concentrated sulfuric acid. The presence of carbohydrates was shown by the production of a purple line at the interface of two portions[9]. This confirms the presence of carbohydrate.

Protein detection (Biuret Test)

An aliquot of 2 ml of 5 % solution biomaterial was shaken with 1 ml. of sodium hydroxide and a few drops copper sulfate solution. The detection of proteins was revealed by the display of violet color after five minutes incubation[10]. This confirms the presence of proteins.

Micromeritic properties characterization

The flow properties of biomaterial were identified through tapped density, consolidation index which was measured with tapped density analyzer, and bulk density apparatus. The angle of repose meanwhile was assumed to be the inverse tangent of the height/base radius of the cone where the flow characteristics was maximized[10]. These all properties define the powder cahracteristics, their particles packing arrangement with the porosity.

Scanning Electron Microscope (SEM)

A JSM-7610F scanning electron microscope was used to analyze the morphology of the surface of the biomaterial. The biomaterial was put on aluminum stubs and shadowed by vacuum gold-coating followed by taking it under various magnifications to present its structure.Then the findings of SEM image was interpreted[11].

Spectroscopy of bio-material

Fourier-transform Infrared (FTIR) Spectroscopy

The functional groups of the biomaterial were identified. This was done by adding KBr pellets and subjecting the mixture to an FTIR analysis. For this 1 mg sample of the isolated biopolymer was dissolved in 100 mg of dried, desiccated solid potassium bromide (KBr), ground in a mortar and pestle, dried in an infrared lamp to remove any residual moisture, pressed into a disc with 10 tons of pressure using a hydraulic pump, and placed in a disc holder18 in the path of the infrared radiation. The spectra were recorded in the range of 4000-200 cm-1[12].

DSC-differential scanning calorimetry

The biomaterial was scanned with DSC calorimeter to measure heat capacity and phase transitions using the thermal analysis method of DSC testing. It measures the rate of heat flow into and out of the sample as a function of temperature. The sample was obtained and underwent a temperature controlled program where the transition temperature for glass transition was determined. The range of heat flow was 50–300°C[12].

Nuclear magnetic resonance spectroscopy

NMR spectroscopy determined the major functional groups of the biomaterials based on their molecular structure. NMR spectroscopy was used to analyze the isolated biopolymer in a particular solvent, CDCl3, high-rate flow of the mixture was injected into the device, the valve switch was used to stop the flow, a measurement was taken, and the spectrum was processed and examined by an automated computer[13].

Mass spectroscopy

The biomaterial was confirmed by mass spectrometry to be polymeric in nature. In this laboratory approach, an intake system introduced the biopolymer sample, and created the compound\'s gas phase ions, which were subsequently fragmented by molecular ion fragmentation in a mass spectrometer to produce an ion abundance versus mass to charge ratio mass spectra[13].

Cytotoxicity testing

Biomaterial cytotoxicity was measured using the SHSY-5Y neuroblastoma cell line cultured in Hams F-12 medium to which fetal bovine serum and antibiotic-antimycotic cocktail were added. To determine the viability of the cell, it was tested through MTT assay to ascertain the safety of biomaterial to be used in pharmaceuticals[13].

Model drug nanosizing

Phenytoin (500 mg) was sonicated 15 times in 25 ml methanol and 25ml of distilled water was added drop wise to precipitate. A milky-white suspnsion with cloudy apppearnce was observed. Centrifugation was done on the suspension acquired, and the nanosized phenytoin was weighed and put back into storage. The percent transmittance, percent blockage, and absorbance were determined after each sonication, with the aim of reducing the particle size[14].

Drug-biomaterial compatibility study

Compatibility with UV spectroscopy was performed between drug phenytoin and biomaterial at different ratios of 1:1, 3:1, 1:3 and 3:3. The solutions were tested in wet (5 %) and dry (100 %) conditions, and maximum absorption (wavelength λmax) was measured in the absence of any chemical interactions that may interfere with the effect of therapy[15].

Preparation of bio-nanodispersion

The bio-nanodispersion was mixed using phenytoin, biomaterial, and excipients (distilled water, 0.5 % polyvinyl alcohol, 0.5 percent sodium benzoate, and 1% dextrose) in the proportions detailed in Table 1. The whole volume was maintained up to 15ml and then sonicated for 15 cycles at 5000rpm with 0.5 % polyvinyl alcohol and 1 % dextrose to enhance particle optimization (16). Dextrose was used as a nanosizant. To increase the nanosized particle It was also tested for refrigeration stability at 48 h, no sediment formation was observed, which indicated optimization [16].

Table 1: Phenytoin-loaded bio-nanodispersion formulation design using cestrum nocturnum biomaterial

Formulations	NSPHNP1	NSPHNP2	NSPHNP3	NSPHNP4	NSPHNP5
Drug : bio-material ratio	1:2	1:4	1:6	1:8	1:10
NSPH (mg)	15	15	15	15	15
CNBM (mg)	30	60	90	120	150
Sodium benzoate (%)	1.0	1.0	1.0	1.0	1.0
Polyvinyl alcohol (ml)	0.5	0.5	0.5	0.5	0.5
Dextrose (%)	1.0	1.0	1.0	1.0	1.0
Double distilled water (ml)	15	15	15	15	15

Bio-nanodispersion characterization

pH and dispersibility

The bio-nanodispersion was prepared using a technique of dispersing 20 mg of nanoparticles in 20 mL of sterile water by sedimentation and redispersion. The dispersibility was measured as function of any agglomerationa or aggregation in the suspension system. The pH was measured using a calibrated pH meter and was observed three times to verify reproducibility[17].

Entrapment Efficiency

Entrapment efficiency was determined by ultracentrifugation of the bio-nanodispersion at 2000 rpm for 10 minutes, and the absorbance of the supernatant liquid at 216 nm was determined using a UV spectrophotometer. This test was performed for three times for the reproducibility. The standard error mean was also calculated.

Particle Size Screening

The particle size screening was performed using UV spectroscopy to obtain volume from the transmittance (the percentage of particles with a volume of less than 400 nm) and more sonication cycles that showed increased transmittance, indicating the effectiveness of nanosizing[17]. After each sonication cycle the transmittance was determined until all the particles were come under 400nm size range.

Particle size analysis with Zetasizer

The Malvern Zetasizer was used to determine particle size distribution and zeta potential to ascertain the stability and nano-range size of bio-nanodispersion. The zeta potential and polydispersity index (PDI) was measured for the optimized formulation[17].

***In-vitro* drug release Study**

All the formulation bionanosuspension (NSPH1-NSPH5) underwent an in-vitro release study using the semi-permeable membrane method of breast milk and the novel method by use of a modified M.S. diffusion apparatus with a static technique of release study on aqueous colloidal media. It consists of two compartment one donor and another receiver compartment. In a donor compartment (2ml) formulation release study was loaded and the end of the donor was coupled with the egg biomembrane. A receiver compartment (14 ml phosphate buffer solution of pH7.4) was immersed in this donor compartment and a 36-hour sampling was conducted on a regular basis. After each sampling, the samples were emptied and refilled with fresh phosphate buffer solutions. The amount of the drug released was determined by UV Spectrophotometer and plotted in a %CDR and time relationship. The other parameters such as r2, t50 and t80 % were calculated. Referring to the results in the in vitro release study of various formulated bionanosuspension (NSPH1-NSPH5) (17) [18].

Stability study

Stability study was conducted using ICH guidelines where bio-nanodispersion was stored at 25°C (60%RH) and 40°C (75%RH) for 6 months and parameters monitored were drug content, pH, color, appearance and entrapment efficiency without compromising the formulation integrity[19,20,21].

RESULTS AND DISCUSSION

Yield of bio-material

he biomaterial was cream-white, with a yield of 10±1.5%. The yield was found to be satisfactory. The color change temperature was 280±2ºC and this indicated good heat stability[20,22].

Physicochemical Properties

It was freely soluble in methanol and water, but not in diethyl ether and acetone. Chemical testing indicated the presence of carbohydrates and proteins, and this suggested that it is polymeric in nature (Table 2).

Table 2: Characterization of isolated biomaterial

Parameters evaluated	Observation
Colour	Brownish-cream
Odour	Characteristic odor
Taste	Characteristic taste
Melting point	280 ±2 ºC.
Solubility	Soluble in water and methanol
Carbohydrate	Present
Protein	Present

Micromeritic properties

The material had acceptable flow properties[20] with a bulk density of 0.86 g/cm^3, tapped density (0.76 g/cm 3), and a consolidation index (12.5 g/cm 3). The biomaterial was found to have a excellent flow property with the angle of repose of 10^0.

Scanning Electron Microscopy

Scanning Electron Microscopy showed flaky and granular surface topography at 5000X. The surface was rough in nature. From the surface morphology and composition study and might be expected for a polymeric material (Figure 1).

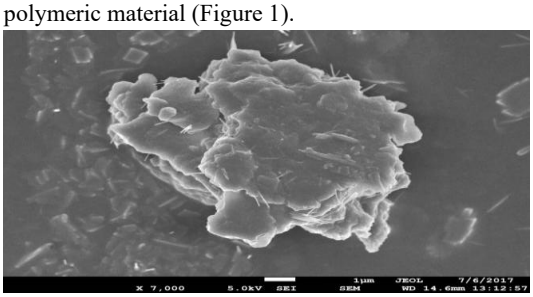

Figure 1: SEM picture of isolated biomaterial at ×5000

Spectral Findings

FTIR spectroscopy

On the basis of FTIR spectroscopy of the isolated biomaterial there is alcoholic OH stretching at 3400.22cm-1,Carboxylic OH stretching at 3019.48 cm-1, C-H bending at 758.04cm-1,C-O stretching at 1215.51 cm-1, C=C stretching at 1621.37cm-1, C-N stretching at 1200cm-1. Its polymeric character is reflected by the presence of the hydroxyl and carboxylic group, and it demonstrates its polymeric nature by the presence of amine and other groups, which have been shown in Figure 2.[20]

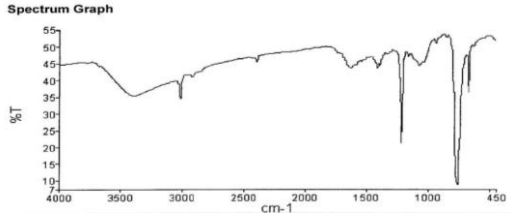

Figure 2: FTIR Spectra of bio-material

DSC Analysis

DSC thermogram of biopolymer extracted in biomaterial showed an endothermic peak at 63.83oC with 98.71mJ/mg. The amorphous nature of the biopolymer was revealed by the DSC spectra[20,21] with a wide endothermic peak Figure3).

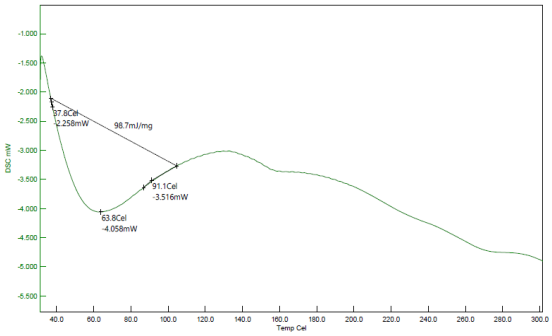

Figure 3: Bio-material thermogram using DSC

Mass spectra

Parent peak at m/z 171.19, confirms its polymeric nature (Figure 4).

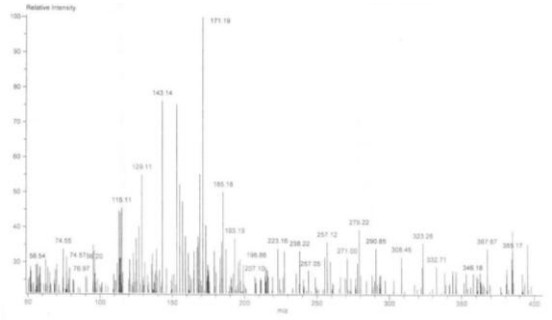

Figure 4: Full-resolution mass spectrum of biomaterial

NMR spectroscopy

The NMR spectra of biomaterial biopolymer shows hydroxyl at 1.255ppm, aromatic at 7.26, methyl -CH3 at 0.901ppm, -CH2 as methylene at 1.333ppm and R-NH2 at 1.557ppm. The presence of these groups like methyl, methylene and hydroxyl aromatic groups confirms its polymeric character[20,21] (Fig. 5).

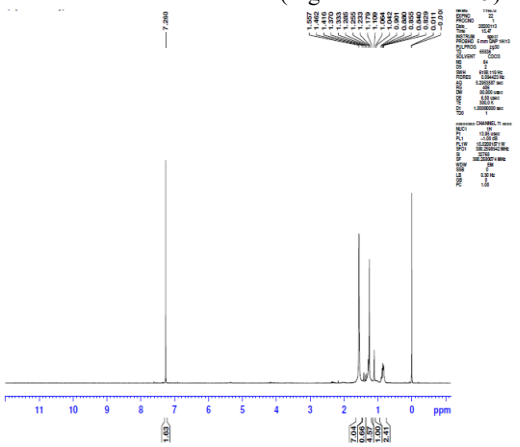

Figure 5: NMR Spectra of biomaterial

Cellline cytotoxicity study

Toxicological testing against cell lines showed an IC50 value of >500 g/ml, with a the overall average % cell viability of 155.34±1.441 to 57.84±1.88, indicating that bio-material was non-toxic when tested using a biomaterial and was thus safe for use in formulation of a drug-loaded bio-nanodispersion. The data from the cell feasibility study can also be used to confirm that the study did not detect cell death, and the measured IC50 value of the bio-material was greater than 100g/ml, indicating that bio-material is safe and non-toxic in its native form[20,21]. Figure 6 shows the relationship between the concentration of bio-material and average % of cells in cell lines viability.

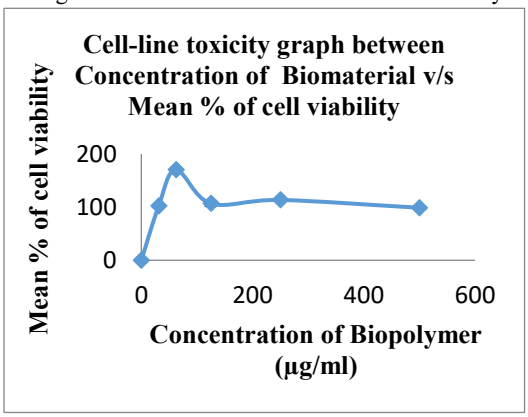

Figure 6: Cell-Line Toxicity Graph of Biomaterial Concentration vs. Mean % Cell Viability

Phenytoin nanosizing

Between a nanosize range, UV screening that demonstrates nanosizing of the model drug-Phenytoin particle size. The percent transmittance of the resultant sample was determined at regular intervals (every three minutes) to ensure that percent delivery increased with increasing sonification cycles, as the particles were nanosized[20,21]. Madhav and Raina (2019) show that a greater proportion of the particles had a diameter greater than 400 nm by blocking (Figure. 7) and a lower proportion of the particles had a diameter less than 400 nm by bio-nanodispersion transmission[20].

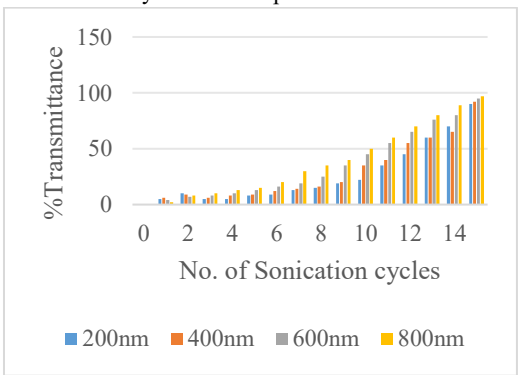

Figure 7: % Transmittance of Measurement and Total % Permeation of Phenytoin through Egg Membrane

Permeability study through biological membrane

The data was analyzed using a UV spectrophotometer to plot a graph of concentration vs. time and determine the amount of drug that permeated through the membrane at different time intervals (Figure 8). The membrane used for the permeation was an egg membrane and this mimics the physiological membrane of the ear, so the phenytoin penetration observation shows that the egg membrane can be used to model the physiological membrane of the ear for drug release studies[20,21].

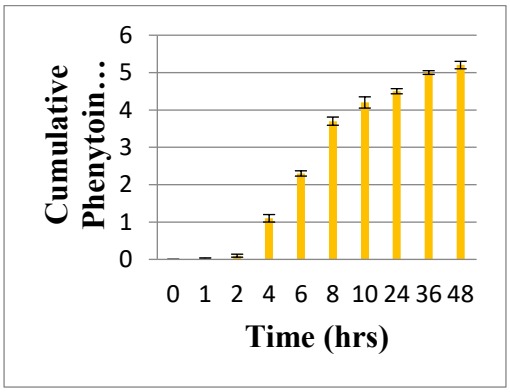

Figure 8: **Cumulative Phenytoin permeation (µg/ml) through egg membrane**

3.9.Drug-Biomaterial Compatibility

The maximum concentration (max) was very close to that of the pure drug and the drug-bio-material combination (216 nm) had the highest wavelength in all cases except when no strength was being analyzed (Madhav and Yadav, 2013). If the maximum did not differ significantly from that of a pure drug, there was no interaction of the drug, the bio-material, and other excipients. We observed that the isolated bio-material that will be used to develop the bio-nanodispersion showed no interaction and transformation of the therapeutic properties of excipients[16,,21].

Drug - Loaded Bio-Nanodispersion Characterization

pH and dispersibility

All formulations, NSPHNP1 to NSPHNP5, were found to have good dispersibility of 7.2 ±0.10 to 7.4 ±0.12 pH units, which is adherent to the physiology (Table 3). The all formulation showed the pH near to physiological fluids which compatible to human physiology[20,21].The best optimized formulation NSPHNP5 showed the excellent dispersibility with pH of 7.4±0.12.

Table 3: Characteristics of NSPHNP1-NSPHNP5

Formulation Code	Dispersibility	Observed pH	Entrapment Efficacy (%)
NSPHNP1	Excellent	7.2±0.10	78.26±0.24
NSPHNP2	Excellent	7.3±0.24	83.17±1.24
NSPHNP3	Excellent	7.4±0.12	88.52±1.00
NSPHNP4	Excellent	7.3±0.26	82.27±1.24
NSPHNP5	Excellent	7.4±0.12	92.47±1.02

Entrapment Efficiency

The bio-nanodispersion prepared had an entrapment efficiency of 78.26±0.24% to 92.47±1.02% (Table 2). The maximum trapping efficiency increased to 92.47±1.02 % for NSPHNP5. Therefore, phenytoin was the best entrapped in the stable bio-nanodispersion NSPHNP5 [20,21].

Particle size analysis

The nanoparticles size of bionanosuspension was determined using Malvern Zetasizer, which showed that the size of the nanoparticles was 133nm. This size and the zeta potential of -7.09mV confirms that the nanoparticles fall within the nanorange which is responsible for the stability of the nanosuspension and also demonstrates that the stable bionanosuspension loaded with phenytoin prepared using Cestrum nocturnum biopolymers is safe for delivery[20,21] to the brain as shown in Figure 9 and 10).

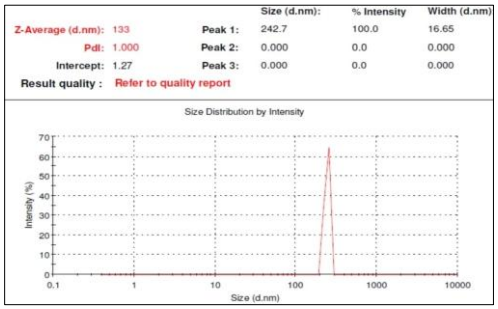

Figure 9: Zeta particle size of NSPHNP5 bionanosuspension

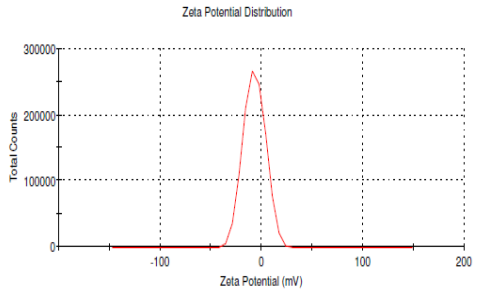

Figure 10: Zeta potential of NSPHNP5 Bionanosuspension

***In-Vitro* release study**

In-vitro release test was carried out using M.S. diffusion apparatus. Release kinetic study was done on the basis of BIT-1.12 software, and t50% and t80%

and r 2 were calculated. In-vitro release study of the drug in all the formulations showed the release percentages of the drug was more than 89.26 % (Figure 10). The drug release profile of different formulations ranged from 89.26 to 99.12% (Figure 11). In-vitro release study of different formulations was performed, and release kinetics was examined. Formulation NSPHNP5 with t50 of 17.26hr and t80 of 31.16 hours with a R^2 value of 0.9899 was the best formulation for use. The best formulation NSPHNP5 showed 89.26% drug release within 36 hrs[20,21].

In the analysis of the release kinetics of different formulations with calculation of t50, t80, and R^2 the percentages of drug releases were above 89.26% in all the formulations, with the same ranging between 89.26% and 99.12% in the various formulations (Figures 10 and 11). NSPHNP5 was the best of the tested formulations, with a t50% of 17.16 hours, t80% of 30.06 hours, and R^2 of 0.9899, which is an excellent fit to the release model, which once again serves as the Higuchi model, with a R^2 of 0.9907. The best percentage of drug release of 89.26% was however recorded by NSPHNP5 in 36 hours implying that it is the best formulation to use to have maximum drug release. Based on the high R^2 values and release profiles, the drug release kinetics can be explained by diffusion-controlled (Higuchi) mechanism with possible addition of concentration-dependent (First Order) and mixed (Korsmeyer-Peppas) assistance by previous R^2 values (0.9907, 0.9865, and 0.9857 respectively). The analysis of the Korsmeyer-Peppas release exponent (n) might further prove the exact release mechanism [20,21].

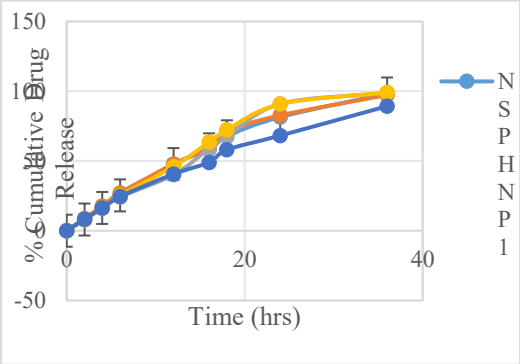

Figure 10: In-Vitro Release NSPHNP1- NSPHNP5

Drug release mechanism with kinetic

Based on the specified R^2 values of the *In-vitro* drug release kinetic models the best formulation NSPHNP5 showed the mixed type of drug release. Higuchi R^2 with 0.9907, the best-fit model suggests that release of the drug is primarily diffusion-controlled and is most likely to follow square-root-of-time release profile. This occurs common in the systems that are of matrix type whereby the drug is diffused through a polymeric or gel like matrix. In First order R^2 with 0.9865, the fit is very good and this means that the release may also have a concentration-dependent effect and the rate of release is directly proportional to the amount of drug available. This normally occurs in systems where the process of dissolution or diffusion is dependent on the concentration of the drug. In Korsmeyer-Peppas R^2 with 0.9857 this model is also very fitting and is applicable with polymeric systems. The high R^2 suggests a process where a combination of release mechanisms (possibly both diffusion and others) occurs[20,21]. It would be the release exponent (n) that determines the mechanism (Fickian diffusion, anomalous transport or case-II transport), however, it is not provided. In Hixson-Crowell R^2 with 9750 this model is least fit which implies that the surface loss or the geometry change of the particles contributes less to the release mechanism. In Zero OrderR^2 with 0.9408 the minimum value of R^2 implies that R 2 is not the most significant mechanism of this drug release. The all type of kinetics have been shown in figure 11.a,b,c,d,e.

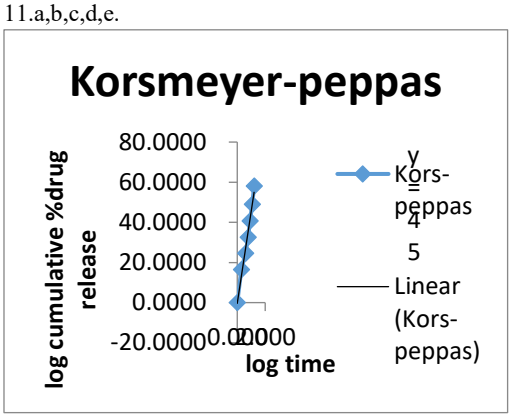

Figure 11:a. Korsmeyer-peppas model

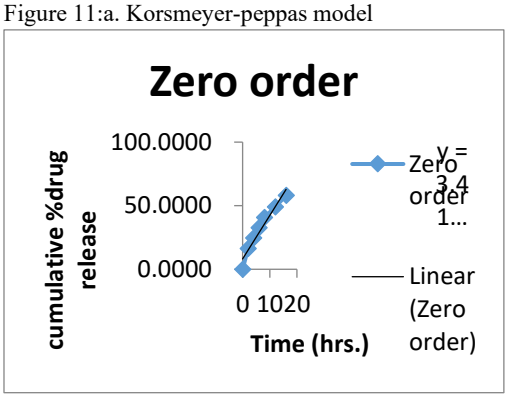

Figure 11:b. Zero-order model

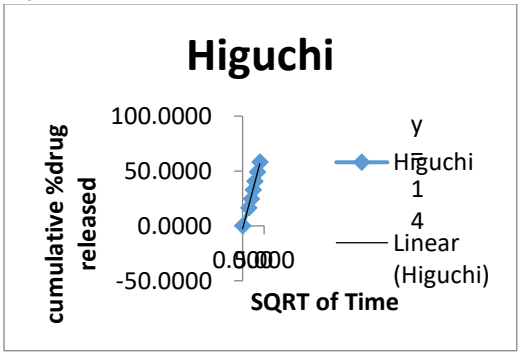

Figure 11:c. Higuchi model

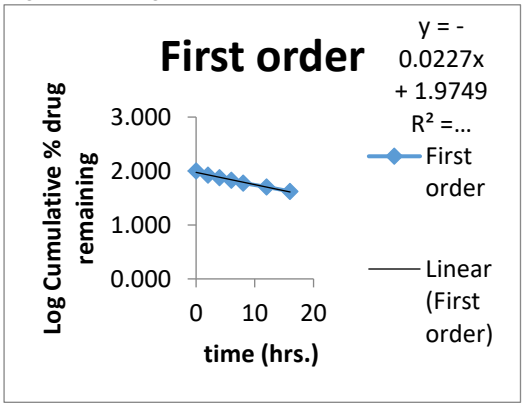

Figure 11:d. First-order model

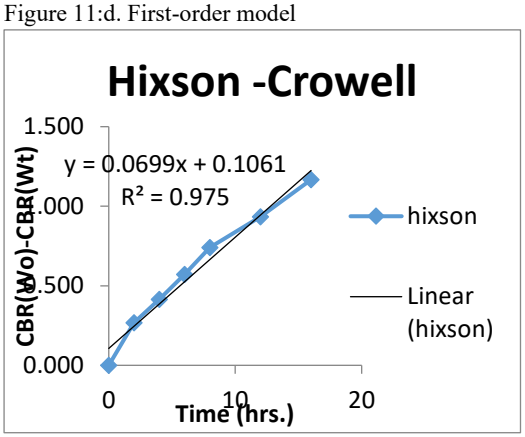

Figure 11:e. Hixson model

Stability of nano-suspension

No change was observed in λmax, entrapment condition, and drug release due to the enhanced details as drawn in table 4. Therefore, no loss of medicine was observed during the study. The results for the rest of the appraisal criteria were also favorable. During the study periods, the most refined formulation, NSPHNP5 was found to sustain its physical and chemical properties without any visible change in color, odor, pH, λmax, %entrapment efficacy and % drug release. t50%

Table 4: Stability study of NSPHNP5

Formulations	Temperature	Parameters Evaluated	Study Periods (Months)						
			0	1	2	3	4	5	6
NSPHNP5	25 °C± 2 °C, 60 %± 5% RH	Appearance	God	God	God	God	God	God	God
		λmax	216 nm	216 nm	216 nm	216 nm	216 nm	216 nm	216 nm
		Changes in color	Milky White	No Change	No Change	No Change	No Change	No Change	No Change
		pH changes	7.4 ±0.01	7.4 ±0.05	7.4 ±0.22	7.3 ±0.55	7.3 ±0.66	7.3 ±0.22	7.3 ±0.67
		%entrapment efficacy	88.52± 1.00	88.25 ±1.11	87.7± 0.21	87.22 ±1.15	86.88 ±1.22	86.45 ±0.81	86.55 ±0.55
		In-vitro release (t50 %)	17.89± 0.22	17.15 ±1.22	18.12 ±0.55	17.69 ±1.22	16.65 ±1.00	16.16 ±1.44	16.05 ±0.44
	40 °C± 2 °C, 75 %± 5% RH	Appearance	God	God	God	God	God	God	God
		λmax	216 nm	216 nm	216 nm	216 nm	216 nm	216 nm	216 nm
		Changes in color	Milky White	No Change	No Change	No Change	No Change	No Change	No Change
		pH changes	7.4 ±0.66	7.4 ±0.22	7.4 ±0.35	7.2 ±0.55	7.5 ±0.43	7.2 ±0.22	7.2 ±0.77
		%entrapment efficacy	88.52± 0.33	88.95 ±0.21	88.60 ±0.14	88.25 ±0.12	87.95 ±0.34	86.65 ±0.23	86.05 ±0.12
		In-vitro release (t50 %)	17.69± 0.1	17.25 ±0.04	17.02 ±0.11	17.25 ±0.8	17.05 ±0.22	16.92 ±0.89	16.62 ±0.13

Chemical and physical stability of the phenytoin-loaded biogenic nano-dispersion was confirmed based on the compatibility and stabilizing potentials of the extracted biomaterial. Problems of a nano-carrier in such development like stability, entrapment efficiency and delivery targeting were satisfactorily addressed. The biomaterial helped to reduce dispersion-related issues due to bio-stabilizing property that resulted in the coherence of formulations[20]. The NSPHNP5 showed good entrapment efficiency with 92.47 ±1.02%, physiological pH of 7.4±0.12 and long sustained release with 89.26% drug release within 36 hrs. In drug to biomaterial ratio of 1:10 and it can hence be considered as a viable candidate to treat epilepsy. The biomaterial can be a possible competitor to synthetic polymers that can be used in new delivery systems due to its degradability and biocompatibility [20,21,22].

CONCLUSION

The research made a phenytoin loaded bio nano-dispersion using the flower petals of Cestrum nocturnum, which has never been done before. The optimized formulation NSPHNP5 displayed slow release of drug over 38hr with great compatibility and efficacy of stabilisation. The evidences support the possibility of the biomaterial to be utilized as a new, non toxic and biodegradable excipient to develop the low cost effective yet effective bio-nanodispersions to treat epilepsy effectively.

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