doi.org/10.36721/PJPS.2024.37.1.REG.085-094.1

Biopolymeric nanoencapsulation of model drug: Its development and characterisation

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Abstract: This research aimed to develop the phenytoin-loaded bionanosuspension by utilising the novel biopolymer from *Juglans regia* andreduce the long-term treatment cost of epilepsy and increase the efficiency of therapy. A novel biopolymer with remarkable inbuilt properties was isolated and used in the development of a nano capsulated dispersed system. The diverse proportions of phenytoin and biopolymer with different ratios 1:2, 1:3, 1:4, 1:5 and 1:8 were taken for the planning of details PJNC1-PJNC5. The bionanosuspension was assessed for dispersibility, pH, % entrapment efficiency, stability study and *in vitro* drug discharge. The formulation PJNC2 with 1:3 drug biopolymer proportion showed significant outcomes for various assessments with $t_{50\%}$ of 16.51 h and r^2 estimation of 0.9884. PJNC2 showed 92.07%±2.5 drug delivery in 36h and was stable. The bionanosuspension was found to be stable and safe for the delivery of nanosized phenytoin utilising the biopolymer having a remarkable stabiliser cum retardant property.

Keywords: *Juglans regia* seeds, biopolymer, bionanoparticles, nanosizing, bionanosuspension, epilepsy.

INTRODUCTION

Polymers assume a vital part in the planning of a novel drug delivery system designed to defeat various complexities in drug conveyance framework planning (Kreutzer J, 2010). These are utilised for controlling the release of the drug in a predetermined manner. The hydrophilic and lipophilic polymers are the best option for getting the ideal delivery in a controlled, sustained, extended manner and delayed delivery at the ideal targets. Separated fromthis, these synthetic and semisynthetic polymers are prepared by various unit operations like chemical treatment measures.

Presently various explorers are being scrutinised for staying away from the high production costs and compatibility issues related to synthetic and semisynthetic polymers. So options, in contrast to manufactured and semisynthetic polymers are being scrutinised with the least unfavourableconsequences for the climate and physiology of the individuals. One of the options in contrast to synthetic and semisynthetic polymers is biopolymers which have attracted the consideration of scientists for planning a novel drug delivery system design (Madhav and Yadav, 2013).

Biopolymers are novel, astute and keen natural polymers, which have been isolated from numerous common sources (Madhav and Ojha, 2014). The nanoparticles are possibly the most liked transporter frameworks for the treatment of CNS issues (Patsalos *et al*., 2002). Since nanoparticles can undoubtedly easily reach the brain by crossing the BBB and targeting of drugs might be accomplished for a delayed time to the desired site (Zhang, 2006). So, the nanoparticles prepared by utilising novel isolated biopolymers are eluded as bionanoparticles as these are biocompatible and biodegradable with an effective drug concentration. Thus phenytoin (anti-epileptic drug) loaded bionanosuspension might be one of the inventive novel drug delivery system designs (Madhav and Ojha, 2014).

Epilepsy is a neurological problem in which the mind movement gets unusual and shows rehashed, uncontrolled and unexpected changes in the brain. In epilepsy, there are strange changes in the electrical movement of the brain (Dawood, 2018). The epileptic scenes are called seizures. There are various factors and conditions which may cause epilepsy in the wake of influencing the brain's electrical discharge in a strange manner (Moschwitzer *et al*., 2004; Muller, 2001; Madhav and Shankar, 2011; Madhav and Yadav, 2013).

In this exploration work, bionanosuspension with the suspended bionanoparticles loaded with nanosized phenytoin has been set up by utilising the novel biomaterial from seeds of *Juglans regia*. The biopolymer was isolated from the seeds of *Juglans regia*. So, the isolated biopolymer from *Juglans regia* might be utilised as an option for prepared synthetic and semisynthetic polymers (Hecq *et al*., 2015; Bennewitz, 2009). This isolated biopolymer is biodegradable and biocompatible in nature.

MATERIALS AND METHODS

Materials

Phenytoin was procured as a gift sample from Affy Pharma Private Limited, Baddi. *Juglans regia* was bought from Yadav general store, Vinhutikhand, Gomtinagar, a

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local market in Lucknow. All other chemicals used were of analytical grade.

Experimental method

Isolation of biopolymer

The *Juglans regia* seeds were purchased from a nearby market. 200 grams of the seed was washed and soaked in distilled water overnight. The swollen seeds were taken and their external covering was removed. The uncovered seeds were ground to paste in a mixer with 100ml of refined water. This slurry was filtered through a muslin fabric. The collected filtrate was centrifuged at 5000rpm for 10 min. After centrifugation, the supernatant was separated and treated with methanol in 1:1 proportions. The mixture was placed in the refrigerator overnight and centrifuged at 5000 rpm for 30 min the next day. The supernatant was disposed of and the biomaterial as sediment was collected and air-dried. This method for isolation of biomaterial was advanced by repeating multiple times and the yield was determined afterwards. The obtained biomaterial was put through sieve number 200 and stored in a desiccator for further utilisation (Tyagi and Madhav, 2019).

Yield of isolated biomaterial

The yield was determined multiple times (n=6) with the assistance of a digital weighing machine. This was determined based on the weight of the isolated dried biopolymer powder to the measure of the crude material utilised for extraction and multiplied by 100. A complete load of isolated biopolymer was noted and %yield was determined with standard deviation.

Characterisation of isolated biopolymer

The physicochemical properties of the isolated biopolymer were portrayed for colour, scent, taste and dissolvability. Synthetic tests to determine the presence of starch and proteins were performed. The confined biopolymer was additionally described for SEM examination, DSC testing, FTIR spectroscopy, mass spectroscopy and NMR spectroscopy. The pH was resolved for 1% watery arrangement with the assistance of a computerised pH metre (Systronics, India). The tests were performed three-fold (n = 3). The solubility study of biomaterial was determined and (n = 3). Particle size analysis of biomaterials was also determined. This was performed by utilising an optical microscopy strategy. During the assessment, around 100 particles were tallied and molecule size conveyance was resolved. This was acted in three-fold and determined.

Determination of rheological properties of biomaterial

Tapped density was determined by subjecting the powder to 20 tappings in a tap density apparatus. The angle of repose was determined for the isolated biopolymer. The point of rest was resolved from the proportion of tan-1 of the proportion of stature of the heap and sweep of the heap. The obtained results were related. The percentage consolidation index was utilised for assurance of stream properties.

Scanning electron microscopy

The isolated biopolymer was analysed by scanning electron microscope (JSM-7610F). A small amount of biopolymer was taken and fixed on aluminium stubs and covered with gold with the assistance of a sputter coater under vacuum. The images were captured at various magnifications.

FTIR spectroscopy, differential examining calorimetry, mass spectroscopy, NMR spectroscopy

The FTIR spectroscopy was finished by setting up the KBr plates. In DSC, testing is the warm investigation method wherein the warmth stream into or out of the example is resolved as the capacity of temperature. The NMR spectroscopy was accomplished for the otherworldly examination of a secluded biopolymer.

Cytotoxicity evaluation of biopolymer on neuroblastoma cell line

Cytotoxicity assessment of disengaged biopolymer was done on the neuroblastoma cell line. The materials utilised were cell line-SHSY-5Y (human bosom malignancy cell line), Ham F-12 media, foetal cow-like serum (FBS), antibiotic-antimycotic arrangement from thermo scientific and MTT reagent from Sigma Aldrich, USA.

Nanosizing of model drug

500 mg of phenytoin was taken and broken up into 25 ml of methanol. The reasonable arrangement was sonicated for 15 cycles persistently. During sonication, 25 ml of purified water was added gradually drop by drop till precipitation was noticed. Then the suspension of phenytoin was allowed for centrifugation. After every sonication cycle, the sample was taken into consideration for absorbance and % transmittance and % blockage (100 -%transmittance) estimation. The buildup was recuperated and afterwards dried to collect the nanosized phenytoin. Then the dried to get the nanosized phenytoin was stuffed and put away for further utilisation. Phenytoin was likewise nanosized by a novel sonication strategy (Tyagi and Madhav, 2019; Tyagi and Madhav, 2019).

Drug-biomaterials interaction studies

The drug-biopolymer interaction study was performed by the U.V. spectroscopy strategy. In the wet technique, the combination of phenytoin and biopolymer in the proportion of 1:1, 1:3 and 3:1 was arranged and wetted with purified water (1 ml) and afterwards dried at 50^{o}C for one hour to eliminate the water content. The dried combination was treated with methanol to dissolve the phenytoin and further λmax was resolved and repeated multiple times. In the dry strategy, the three different proportions of drug-biopolymer, same as the wet

technique, were arranged and afterwards treated with methanol to break down the phenytoin and further λmax was resolved (Madhav and Tyagi, 2019).This was rehashed multiple times. λmax was analysed when the test for any change.

Formulation bionanosuspension

The details of bionanosuspension preparation by utilising different drug biopolymer proportions are given in table 1. The bionanosuspension was prepared by sonication of the combination of drug and biopolymer alongside other excipients like polyvinyl alcohol as suspending agent, sodium benzoate as the preservative, purified water and dextrose as the nanosizent. Phenytoin, *Juglans regia* biopolymer and other excipients were precisely weighed and powdered and mixed with a little purified water. This blend was sonicated for 3 cycles. At that point, 0.5 ml of 0.5 % polyvinyl alcohol was added during sonication. The volume was made up to 10ml with double distilled water having sodium benzoate with 0.5%. Add dextrose to 10 mg as a nanosizing agent and took into consideration sonication for 15 cycles. After sonication, the bionanosuspension was refrigerated for two days. Assuming no settlement is there, it implies the detailing is optimised. On the off chance that settlement is there, 0.5 ml of 0.5 % polyvinyl alcohol was again added and allowed for sonication for 10 cycles and refrigerated for 48 hours. The various formulations were prepared and after optimisation PJNC1 - PJNC5 were prepared. After preparation, the following parameters were accessed in the characterisation of drug-loaded bionanosuspension with suspended nanoparticles (Tyagi and Madhav, 2019).

Characterization of Bionanosuspension

Dispersibility and pH

20 mg of the detailed nanoparticles was taken and suspended in 20ml of distilled water in a test tube. The ideal opportunity for settling of the suspended nanoparticles at the bottom was noted and afterwards, again the nanoparticles were redispersed and observed for the redispersion. In the wake of shaking, any lump or precipitation development was noticed. The procedure was repeated thrice and observed. The pH of planned bionanosuspension was assessed with an advanced pH metre. The investigation was done three-fold and the mean was taken and watched to see whether the pH of the nanosuspension is within required reach or not.

Entrapment efficacy

The entrapment efficacy was determined for the prepared bionanosuspension. The newly prepared bionanosuspension was taken and centrifuged at 2000 rpm in an ultracentrifuge. After centrifugation, the supernatant was taken and weakened and the measure of the drug unincorporated was estimated by deciding the absorbance under UV spectroscopy at 216nm. This assurance was done three-fold and normal was determined.

Particle size screening of bionanosuspension

The bionanosuspension was evaluated by measuring the transmittance of the bionanosuspension. The transmittance was measured as a function of the particle size in the nano range done by the sonication method. The % transmittance depends on the particle size range at the particular range that defines the size of particles below the range and the size of the particles beyond the range required. The % transmittance was determined before and after the sonication cycle. The effect of sonication on % transmittance was observed after sonication and measuring the % transmittance after each sonication cycle (Madhav and Tyagi, 2019).

In vitro drug release study

The *in vitro* release study was performed for all detailing. *In vitro* release study was performed by a novel static technique by utilising M.S. (Madhav-Shankar) diffusion apparatus. It comprises two compartments- one donor and one collector compartment. The formulation for the release study was taken in the donor compartment (1ml) and the end of the donor was tied with the egg biomembrane. This donor compartment was immersed in the receiver compartment having 13 ml of pH 7.4 phosphate buffer solution. Sampling was done at different specific time intervals for 36 hours. The samples were withdrawn completely and replaced with fresh phosphate buffer solutions after every sampling (Tyagi and Madhav, 2019). The samples were analysed by UV Spectrophotometer for determining the released amount of the drug. The graph was plotted between the %CDR and time. The other parameters like r^2, t50 and t80% were calculated for evaluation of release study, kinetic study for different formulations and selection of best-optimised formulation.

Stability

The stability study was preceded according to ICH rules. The formed bionanosuspension was put away at various temperatures for half a year. The bionanosuspension was kept at two unique conditions at 25ºC ±2ºC, 60% RH and 40±2ºC, 75% RH in a stability chamber. The samples were noticed at regular intervals for their various parameters during the testing period. The formulated bionanoformulations under assessment were noticed for the drug content, pH changes and furthermore any change in its colour, appearance, encapsulation efficacy and *in vitro* release (Tyagi and Madhav, 2019).

STATISTICAL ANALYSIS

Finding a mathematical expression that can explain the release mechanism of drug from various bionanosuspension formulations was the primary goal of this statistical analysis. To determine the optimal formulation with significant drug release, the release

kinetics were investigated using the software BIT-SOFT 1.12 version.

RESULTS

Appearance, yield, colour changing point of isolated biomaterial

The isolated *Juglans regia* biopolymer showed a whitish-cream shading. The yield of isolated biopolymer was observed to be 8±1.2%.The colour changing point was observed to be 275±4ºC. This implies that a critical yield was isolated from the natural kernels.

Physicochemical properties of isolated biopolymer

In physicochemical portrayal, the taste of biopolymer was observed to be characteristic. The biopolymer was soluble in water and methanol and observed to be insoluble in acetone and diethyl ether. The tests for starch and protein showed positive test in chemical testing for these constituents. The presence of these high molecular weight constituents uncovers that these are polymeric in nature. The perception of various parameter discoveries of segregated biopolymer of *Juglans regia* is summarised in table 2.

Particle size analysis of biomaterial

The particle size of the isolated biopolymer was to be found in the scope of 54.32-314.8µm. The outcome uncovers that the biopolymer is granular in nature with a flaky appearance with changed molecule size. The flaky appearance with granular construction was likewise related to the SEM picture. The particles noticed were observed to be like the standard polymers.

Rheological properties of biomaterial

The distinctive rheological properties like bulk density were found to be 0.66±012 g/cm3, tapped density 0.9±0.11g/cm^3, consolidation index with 13.5±1.2%, which indicated agreeable outcomes. Hence, the isolated biopolymer was found to be free-flowing and appropriate for the preparation of bionanosuspension.

Scanning electron microscopy

The scanning electron microscopy examination of the isolated biopolymer structure *Juglans regia* showed a flaky and granular surface. Such granular and flaky designs affirm its polymeric nature (Madhav and Yadav, 2013). The SEM picture of the secluded biopolymer is shown in fig. 1.

FTIR spectral characterisation, differential scanning calorimetry, mass spectroscopy and NMR spectroscopy

The FTIR spectral examination of biopolymer announced the presence of functional groups like hydroxyl (3395.29cm^{-1}), alkynes (668.01cm^{-1}), carboxylic group (1386.63 cm^{-1}) and furthermore other groups like amide at 1638.82 cm^{-1}, alkenes at 2926 cm^{-1} (Tyagi and Madhav, 2019). The presence of these functional groups is liable for its polymeric nature like other prepared and semisynthetic polymers. The FTIR spectrum is shown in fig. 2.

The DSC of biomaterial from *Juglans regia* showed peaks at 83.27ºC and 128.3ºC. The area was found to be 18.24 mj/mg and 0.55 mj/mg separately (Madhav and Yadav, 2013). The obtained result affirms its polymeric nature. The broad endothermic peak uncovers its polymeric nature as demonstrated in fig. 3.

Mass spectra examination of the isolated biomaterial uncovers that the confined biopolymer is polymeric in nature because of the quality of high molecular weight structure. The presence of a great molecular weight affirms the presence of proteins. The high-resolution mass spectra of isolated biopolymers showed the parent peak at m/j 579.29 (Madhav and Yadav, 2013). Its high molecular weight demonstrates its polymeric nature as shown in fig. 4.

The NMR spectra show the presence of peaks such as the peak at 0.90ppm which uncovers the presence of alkyl group, peak at 1.25ppm confirms the presence of methylene group, at 1.26ppm shows the presence of hydroxyl group, at 2.3ppm affirms the presence of ester group, at 4.2ppm uncovers about aliphatic methylene proton (Tyagi and Madhav, 2019). The presence of these groups affirms its polymeric nature as shown in fig. 5.

Cell line toxicity

The cell line toxicity test results of biomaterial from *Juglans regia* of 0.31.25, 62.25, 125,250 and 500 (µg/ml) showed the mean % cell viability going from 152.38±2.72% to 58.843± 9.27% with IC50 value of >500 µg/ml. In this way, the cell feasibility measures information that exhibits that there is no cell death seen in the examination. Alongside this, the IC50 estimation of the biopolymer was above 100 µg/ml. The acquired information confirmed that biopolymer was discovered to be protected and non-harmful in nature. So, it may be securely utilised for the arrangement of drug-loaded bionanosuspension. Cell-line toxicity graph of concentration of biopolymer versus mean % of cell viability is shown in fig. 6.

Nanosizing of phenytoin

In nanosizing, the phenytoin particle size was found to change in nanosize range which was affirmed by UV screening. During the nanosizing of phenytoin after every sonication cycle (each cycle equivalent to three minutes), the sample was noticed for % transmittance that affirmed that as the quantity of cycle expands the % conveyance was expanded. This was because the particles are now converted into nanorange. Transmittance indicated % of particles below 400 nm in bionanosuspension and % blockade give an idea about the particles which are above 400 nm (Madhav and, 2017) (fig. 7).

Table 1: Formulation design of phenytoin loaded bionanosuspension using *Juglans regia* biopolymer

Formulations	PJNC1	PJNC2	PJNC3	PJNC4	PJNC5
Drug : biopolymer ratio	1:2	1:3	1:4	1:5	1:8
Phenytoin (mg)	10	10	10	10	10
Juglans regia (mg)	20	30	40	50	80
Sodium benzoate (%)	0.5	0.5	0.5	0.5	0.5
Polyvinyl alcohol (ml)	0.5	0.5	0.5	0.5	0.5
Double distilled water (ml)	10	10	10	10	10

Table 2: Characteris ation of Isolated Biopolymer of *Juglans regia*

Parameters evaluated	Observation
Colour	White-cream
Odour	Characteristic
Taste	Characteristic
Melting Point	275ºC ±4ºC.
Solubility	Soluble in water and methanol
	Insoluble in acetone and diethyl ether
Carbohydrate	Present
Protein	Present

Table 3: Characteristics of PJNC1-PJNC5

Formulation Code	Dispersibility	Observed pH	Entrapment Efficacy (%)
PJNC1	+	7.4±0.18	85.19±1.9
PJNC2	+	7.2±0.21	84.27±1.14
NJNC3	+	7.4±0.12	75.46±0.5
PJNC4	+	7.1±0.16	80.17±1.14
PJNC5	+	7.3±0.34	85.17±1.1

Table 4: Kinetic model fitting in PJNC1-PJNC5

Formulation	Zero - order	First - order	Higuchi matrix	Korsmeyer-Peppas	Hixon Crowell model	n	Best fit model	Mechanism of release
	r^2	r^2	r^2	r^2	r^2			
PJNC1	0.9702	0.9373	0.9075	0.985	0.9861	0.8228	Koresmayer Peppas	Anomalous Transport
PJNC2	0.9652	0.9453	0.9072	0.9884	0.9862	0.7947	Koresmayer Peppas	Anomalous Transport
PJNC3	0.971	0.9099	0.906	0.9906	0.9739	0.8027	Koresmayer Peppas	Anomalous Transport
PJNC4	0.9161	0.9475	0.9178	0.9781	0.9936	0.8176	Hixon Crowell	Anomolous Transport
PJNC5	0.9184	0.9889	0.9185	0.9744	0.9854	0.8227	First Order	Anomalous Transport

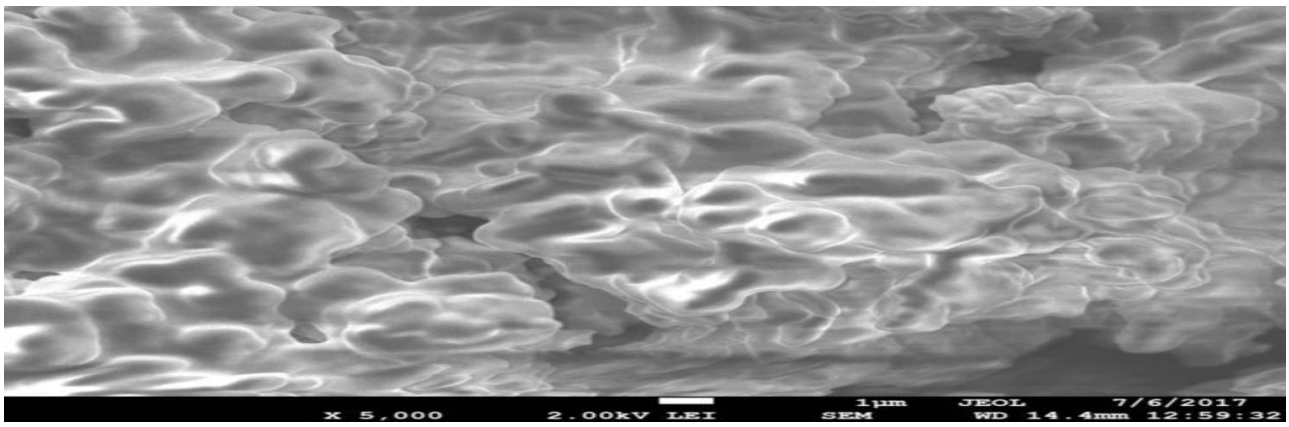

Fig. 1: SEM image of isolated biopolymer of biopolymer from *Juglans regia* at 5000X

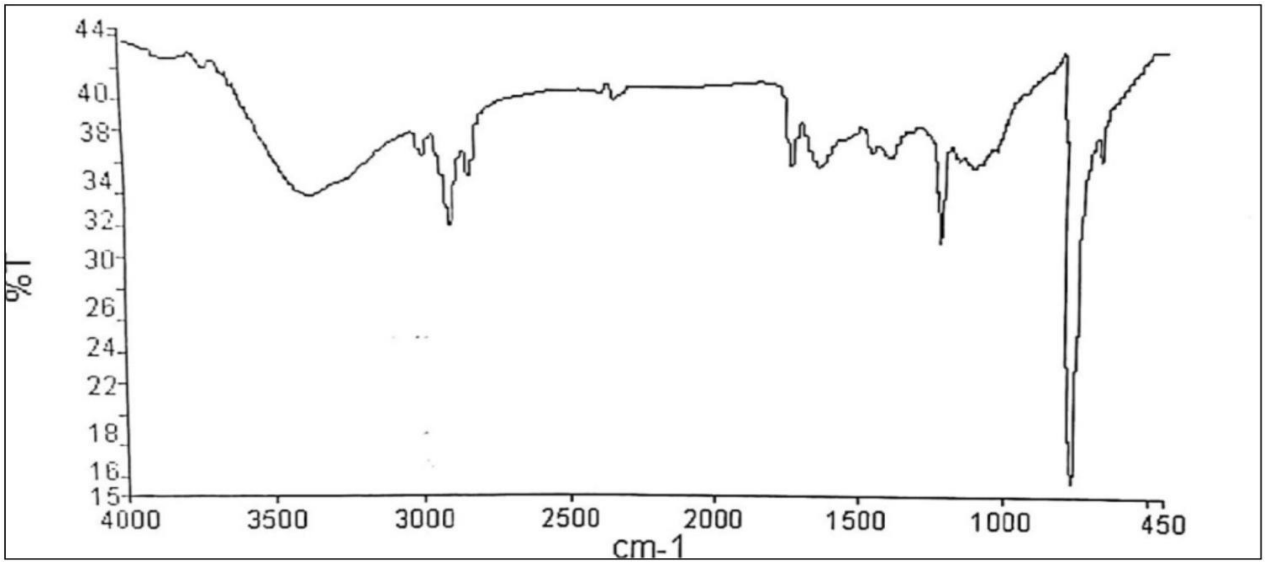

Fig.2: FTIR Spectra of biopolymer from *Juglans regia*

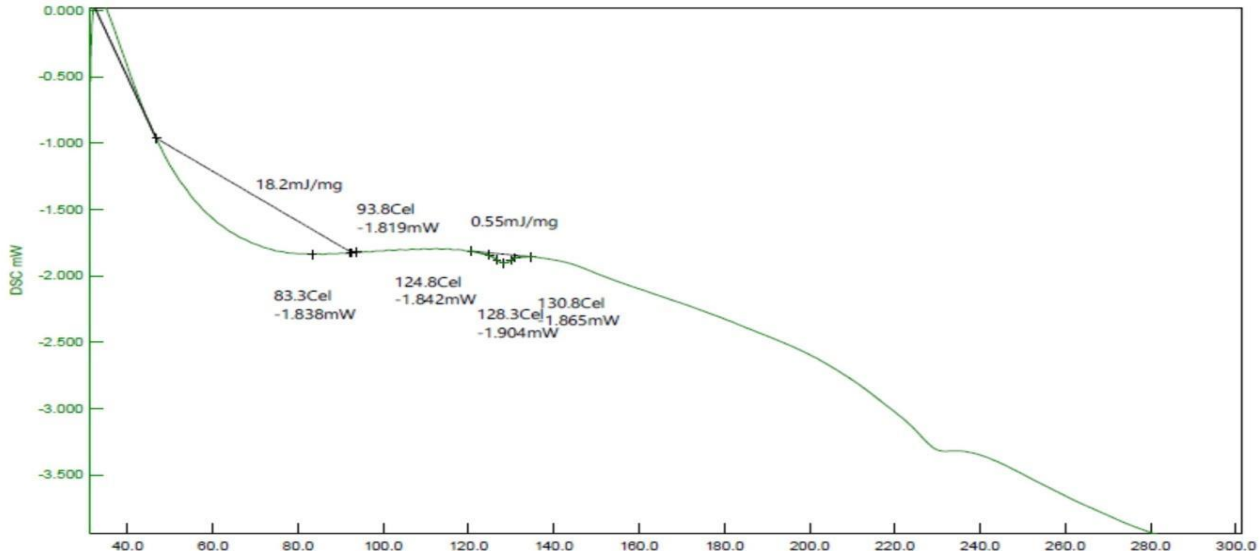

Fig.3: DSC of biopolymer from *Juglans regia*

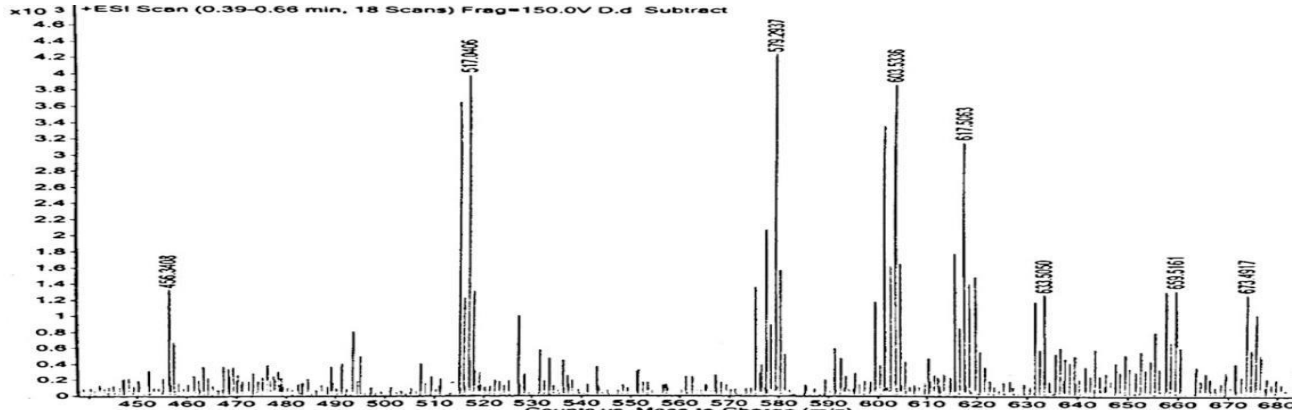

Fig.4: High-resolutionMass Spectrum of isolated biopolymer from *Juglans regia*

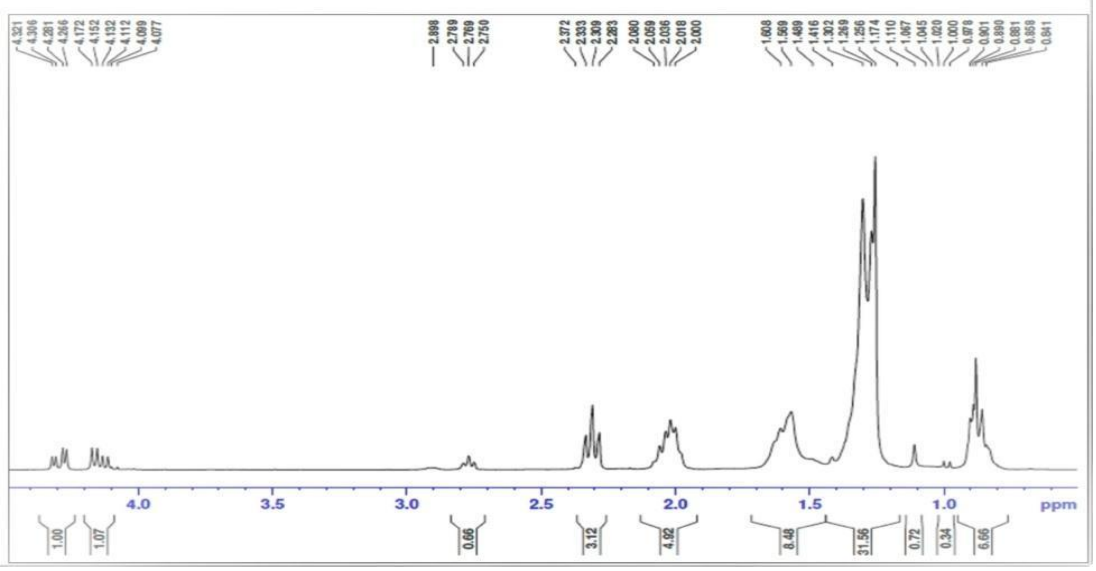

Fig.5: NMR Spectra of biopolymer from *Juglans regia*

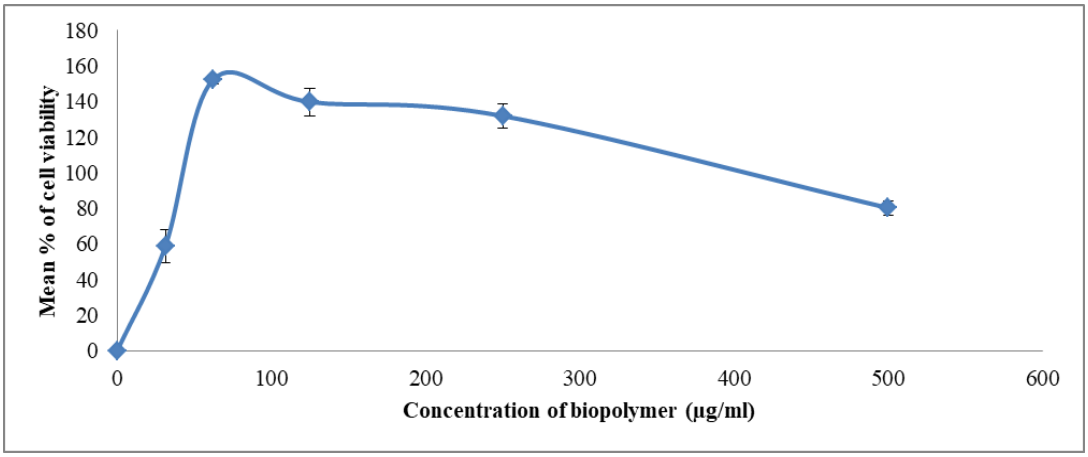

Fig. 6: Cell-line toxicity graph of concentration of biopolymer versus mean % of cell viability.

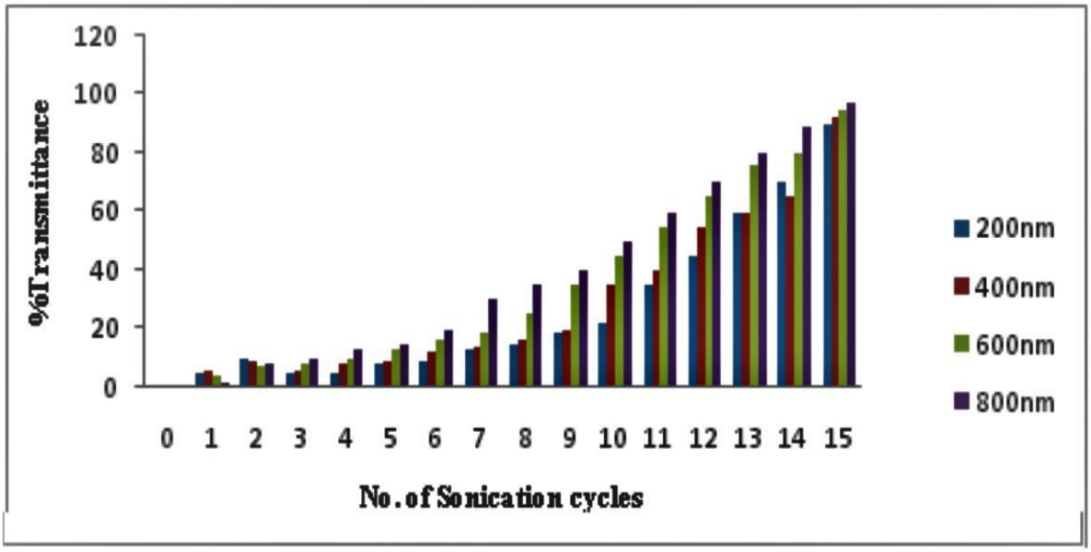

Fig. 7: % Transmittance measurement

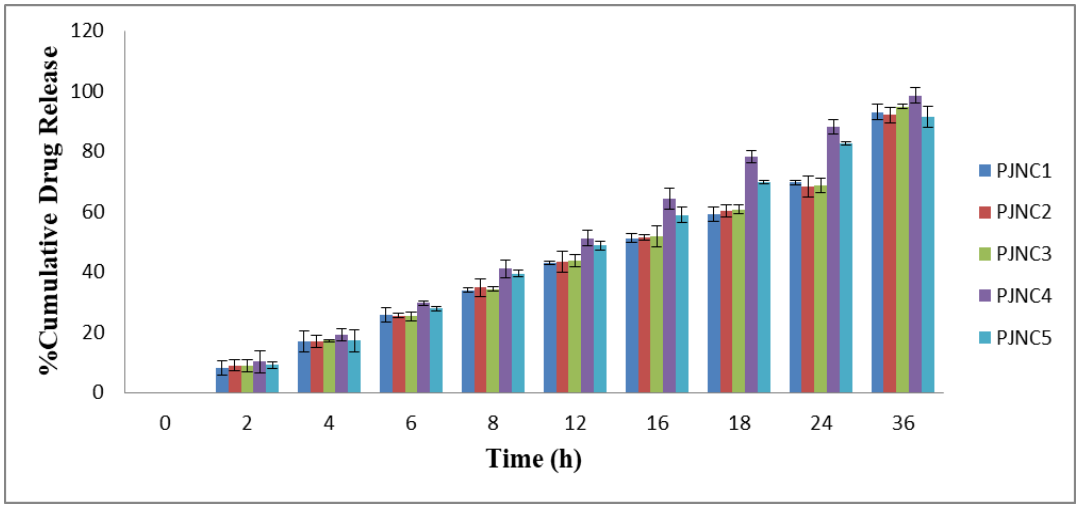

Fig.8: *In vitro* release drug profile of bionanosuspension PJNC1-PJNC5. The results are expressed as mean ± SD (n=3)

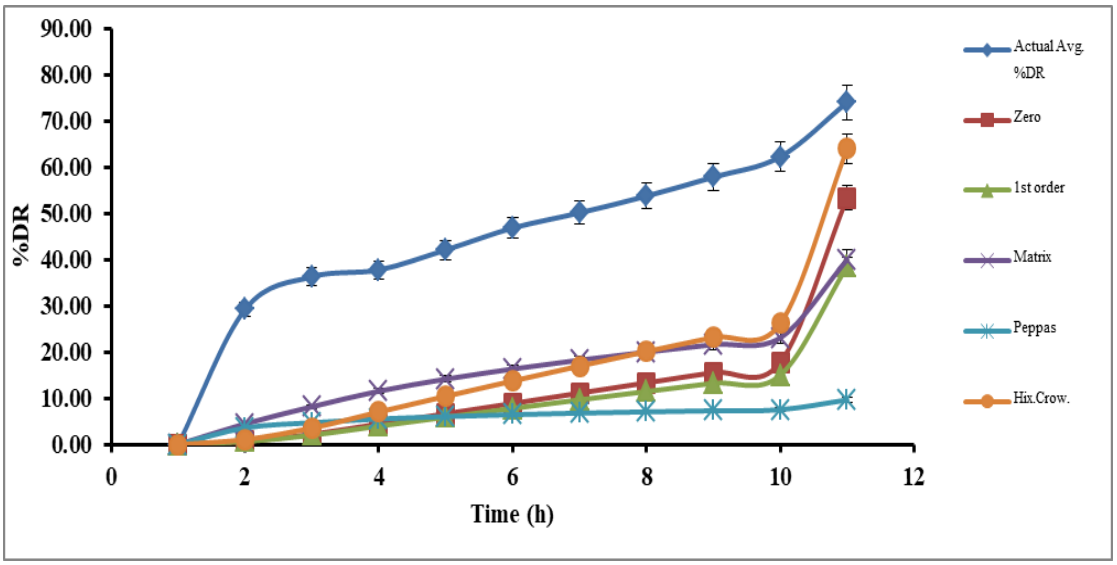

Fig. 9: Model fitting graph for formulation PJNC2

Drug-biomaterial interaction

There was no critical change in λmax previously (216 nm) and after the test (216 nm) in drug excipients study. The λmax was found to be very close to the drug-biopolymer (Madhav and Yadav, 2013) mixture as that of a pure drug. It means that there was no interaction between the drug and biopolymer and other excipients because there was no significant difference in λmax from that of a pure drug. It was noticed and affirmed that excipients aren't interacting and producing any changes in drug properties so that the isolated biopolymer can be utilised for the planning of bionanosuspension (Madhav and Raina, 2017).

Characterisation of phenytoin loaded bionanosuspension

The bionanosuspension with various drug-polymer proportions (PJNC1-PJNC5) were prepared. These chosen PJNC1-PJNC5 were assessed for various parameters like dispersibility, pH studies, % efficacy, screening of bionanosuspension particle size by UV screening and *in vitro* release study. The results are depicted below.

Dispersibility and pH

The dispersibility of the formed bionanoparticles showed good outcomes. The redispersion was additionally determined to be acceptable (Tyagi and Madhav, 2019). All bionanocapsules were found in a scattered state during the scattering study (table 2). No conglomeration or irregular arrangement was noticed.

The pH of the bionanosuspensions was found to be in scope of pH 7.1±0.16 to 7.4±0.18 (table 2). This implies the definitions were in the required pH range that is appropriate for the suitability of the formulated bionanocapsules (Madhav and Raina, 2017).

Entrapment efficacy

The ensnarement viability of the formulated bionanosuspension was found in the reach of 75.46±0.5 % to 85.19±1.9% (table 2). Thus, the defined bionanosuspension showed the greatest entrapment efficacy up to 85.19±1.9. Consequently, the formed stable bionanosuspension showed the greatest entrapment of phenytoin (Tyagi and Madhav, 2019).

Particle size screening

Screening of the formulated bionanosuspension PJNC1-PJNC5 showed all the particles in the nano range. UV strategy was utilised for screening the size of the nanoparticles in bionanosuspension after sonication. As the sonication cycle was increased, the % transmittance was found to be increased on the grounds that the molecule size after sonication has come in the nano range. The transmittance demonstrated the particles below 400 nm and the % barricade showed the % of particles over 400 nm when screened by UV spectrophotometry (Madhav and Raina, 2017).

In vitro drug release

The i*n vitro* release study was performed by utilising modified M.S. diffusion apparatus. The release kinetics examination was finished by utilising the BITS-SOFT1.12 and $t_{50\%}$ and $t_{80\%}$, r^2 were determined. All the formulations showed more than 91.59 % ± 3.5 drug release (fig. 8). The *in vitro* release investigation of various formulations showed drug release from 91.59 %±3.5 to 98.61% ± 2.5. The bionanocapsule PJNC2 was found to be the best formulation having $t_{50\%}$ of 16.51 h with r^2 estimation of 0.9884 with 92.07 % ± 2.5 drug delivery in 36 h. The kinetic studies (table 3) uncovered that best-fit model was Korsmeyer Pappas and the system of drug discharge was found to be anomalous transport. The bionanosuspension arranged with 1:3 proportions of drug and biopolymer showed a critical release of phenytoin. The consequence of *in vitro* release study and release kinetic of all the formulations demonstrates the supported delivery (Tyagi and Madhav, 2019; Madhav and Raina, 2017) of the phenytoin was accomplished from the stable PJNC2. Subsequently, the isolated biopolymer from seeds of *Juglans regia* was found to have critical delivery rate controlling ability with magnificent inbuilt bioretardant cum stabiliser property. In this manner, drug and biopolymer with 1:3 ratio (PJNC2) proportions showed significant release of phenytoin among all formulations.

PJNC2 showed that the best-fit model is Korsmeyer-Peppas as shown in fig. 9 for different models graph, with the mechanism of drug release to be anomalous transport. This uniqueness is the consequence of the novel inbuilt bioretardant property of biopolymer which addresses the issue of long-term epilepsy treatment.

Stability

The upgraded details showed no change in λmax, ensnarement adequacy and in drug discharge. So, there was no drug loss during the examination time frame. The other assessment parameters likewise showed a good outcome. The best streamlined formulation PJNC2 was found to be stable during the investigation time frames with no change in physical and chemical properties. There was no change in colour, odour, pH and physical appearance (Tyagi and Madhav, 2019). During the examination time frame, acquired outcomes affirmed that the formulation was physically and chemically stable and compatible with isolated biopolymer.

DISCUSSION

There are various difficulties which may be encountered during the formulation of nanocarriers. like the stability issues, drug entrapment efficacy and delivery of the drug moiety on the desired site. In this exploration, we have planned a phenytoin-loaded bionanosuspension with dispersed nanoparticles by utilising a novel biopolymer isolated from *Juglans regia* seeds. By developing bionanosuspension, the big issue with any dispersion system was minimised up to a significant level because of its inbuilt bio-stabilising properties (Tyagi and Madhav, 2019). The formulation of bionanosuspension loaded with nanosized phenytoin showed acceptable stability. The utilisation of nanosized phenytoin for preparation of the bionanosuspension showed a fantastic outcome either in the delivery of phenytoin up to the all-encompassing time or during the stability time frame (Tyagi and Madhav, 2019). In this way, in the formulation of bionanosuspension, the novel biopolymer assumed a vital bioexcipient (Madhav and Raina, 2017). The bionanosuspension PJNC2 with 1:3 drug biopolymer proportion, showed the agreeable outcome with huge capture adequacy (84.27% ±1.14), pH (7.2±0.21), drug release (92.07%±2.5in 36 hours) and significant stability. The outcomes uncover its compatibility with phenytoin in bio-nanosuspension form. From these findings, the biopolymer from a regular source can be a novel bioexcipient for the formulation of stable bionanosuspension. Biopolymer from common sources remains an alternative option in contrast to standard synthetic and semisynthetic polymers on account of their biodegradability and biocompatibility (Tyagi and Madhav, 2019; Tyagi and Madhav, 2019,18] with various inbuilt properties. Biopolymer is one of the astounding biomaterials which is available naturally. However, its curiosity has not been investigated expansively. But nowadays, the biopolymer can be securely utilised as a novel biomaterial for developing bionanosuspension with dispersed drug-loaded bionanoparticles for delivery of nanosized phenytoin to the objective site for long-term treatment of epilepsy (Bennewitz and Saltzman, 2009).

CONCLUSION

In this exploration, the bionanosuspension loaded with phenytoin was developed by utilising the biopolymer isolated from the seeds of *Juglans regia*. The optimised bionanosuspension PJNC2 showed significant drug discharge for more than 36 hours. In this way, isolated biopolymer showed a magnificent compatibility with phenytoin and has the critical bioretardant cum stabilising property. The results uncovered that the isolated biomaterial having various encouraging attributes might be utilised as a novel biomaterial for the development of bionanosuspension for the treatment of epilepsy in a very economical and efficient way.

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