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Research article

Formulation and evaluation of nanosized aripiprazole-loaded bionanogels using novel bio-retardant from bark of *Cinnamomum verum* J.Presl

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ABSTRACT

The current research work aimed to formulate and evaluate the aripiprazole bionanogel using *Cinnamomum verum* J.Presl Syn. *C. zeylanicum* (Lauraceae) as bio-retardant and bio-stabilizer for transcranial delivery. Aripiprazole, a partial dopamine agonist is an antipsychotic drug used in the treatment of schizophrenia, bipolar disorder, major depressive disorder, and irritability associated with autism. The biopolymer from *C. verum* was isolated by addition of an optimised quantity of acetone and used as bio-retardant and bio-stabilizer to prepare aripiprazole-loaded bionanogels. The initially aripiprazole nanoparticles were prepared by addition of dextrose and dextran as a nanosized agent and various proportion of bio-polymer *C. verum* as bio-retardant (0.4%, 0.6%, 0.8% and 1%) and guargum (1.5% and 2%) followed by optimised cycles of sonication. The nanoparticles were incorporated uniformly into the gel under magnetic stirrer mode which was prepared by sodium alginate (100 mg), PVA (100 mg) and HPMC (100 mg) and prepared bionanogel was found as the best formulation based on comparison of mentioned parameters i.e. pH, texture, spreadability, % entrapment efficacy, preliminary determination of nano size distribution and in-vitro drug release study. FC3 (1:0.8) containing a retardant showed uniform spreadability, smooth texture and T50% of 51 h and T80% of 72 h, respectively. These formulations can be used for transcranial drug delivery to target the molecule to the brain through the layers of skin, meninges, trigeminal nerves, emissary veins, cranial bones and sutures.

INTRODUCTION

Aripiprazole, a partial dopamine agonist, belongs to the class of antipsychotics that is primarily used in the treatment of schizophrenia, bipolar disorder, and irritability associated with autism. It exhibits high affinity for dopamine D2 and D3, serotonin 5-HT1A and 5-HT2A receptors, whereas moderate affinity for dopamine D4, serotonin 5-HT2C and 5-HT7, α-1-adrenergic and histamine H1 receptors, and serotonin reuptake site (Uzun et al., 2005). This drug has no significant affinity for cholinergic muscarinic receptors. It clinically helps patients by transiently occupying D2 receptors and then rapidly dissociating to allow normal dopamine neuro-transmission. It keeps prolactin levels normal, spares cognition, and obviates EPS. The 5-HT2A receptors are readily blocked at low doses of most atypical antipsychotic drugs except remoxipride and amisulpride (Seeman, 2002). The term transcranial route means the brain targeted a transfer of drug molecules across the cranium through the layers of the skin and skin appendages of the head, arteries and veins of the skin of the head, cranial bones along with the dipole, cranial bone sutures, meninges and specifically through the emissary veins (Pathirana et al., 2006). The unique anatomical arrangement of blood vessels and sinuses in the human skull and the brain, the prevalence of a high density of skin appendages in the scalp, extracranial vessels of the scalp communicating with the brain via emissary veins and most importantly, the way that the scalp is used in treating diseases associated with the brain show that a drug could be transcranially delivered and targeted to the brain through the scalp (Kamila et al., 2014). The emissary veins draining blood from extracranial sites into the intracranial sinuses pierce a series of foramina present in the cranial bones. Scalp veins communicate with sinuses of the brain via emissary veins. There are thirteen emissary veins connecting extracranial sites of the head with intracranial sinuses (Kamila et al., 2015).

The nanogel is prepared from nanosized particles formed by cross-linked polymers. It was

first introduced to define cross-linked bifunctional networks of a polyion and a nonionic polymer for delivery of polyethyleneimine (PEI) and polyethyleneglycol (PEG) (Kabanov and Vinogradov, 2008). The sudden outbreak in the field of nanotechnology have introduced the need of nanogel systems which proven their potential to deliver drugs in controlled, sustained and targetable manner. With the emerging field of polymer sciences, it has now become inevitable to prepare smart nanosystems which can be used for treatment as well as clinical trials.

The nanogels are superior drug delivery system than others because the particle size and surface properties can be manipulated to avoid rapid clearance by Phagocytic cells, allowing both passive and active drug targeting. A controlled and sustained drug release at the target site is improving the therapeutic efficacy and reducing side effects. The drug loading is relatively high and may be achieved without chemical reactions; this is an important factor for preserving the drug activity (Mohanraj and Chen, 2006).

MATERIALS AND METHODS

Isolation of biomaterial

The bark (100 gm) of *C. verum* (Vern. Dalchini) was procured from the market. The biomaterial was soaked in the distilled water for overnight and ground in the grinder for making a paste. The biomaterial was soaked in 100ml of chloroform and kept for 1hrs for removal of oil. Then chloroform was removed through muslin cloth from the biomaterial. Then, 500 ml of distilled water was added in the biomaterial for soaking and kept for 24 h in the refrigerator for the settling of sediment. The supernatant of biomaterial was taken and centrifuged at 3000 rpm for a period of 15 min. After centrifugation, the supernatant was taken and (equal amount of biomaterial) 500 ml of methanol was added after optimisation and kept for 24 h in the refrigerator. Then biopolymer was separated from methanol and spread on the glass plate for air drying. After drying, the biopolymer was scrapped to the glass plate and the bio-material was passed through sieve #120 stored at room temperature. The biopolymer extraction was repeated 6 times and practical yield was calculated.

Formulation of aripiprazole bionanogels

The initially Aripiprazole nanoparticles prepared by addition of dextrose and dextran as a nanosizant and various proportion of biopolymer *C. verum* as bio-retardant (0.4%, 0.6%, 0.8%, 1%) and Guargum (1.5%, 2%) followed by optimised cycles of sonication. The nanoparticles were incorporated uniformly into the gel under magnetic stirrer mode which was prepared by sodium alginate (100 mg), PVA (100 mg) and HPMC (100 mg).

The drug was nanosized by using bath sonicator for 8 cycles (each cycle for 3 min) similarly biomaterial *C. verum* in different ratio was nanosized which was dried in a petri dish. 10 mg of drug was accurately weighed and the varied ratio of *C. verum* biomaterial as biostabilizer and bioretardant was mixed together for each formulation with the addition of 10 ml of distilled water then it was subjected to sonication for 8 cycles. The above solution was poured into the glass pestle and after optimisation, the gelling composition were added viz. sodium alginate (100 mg), PVA (100 mg) and HPMC (100 mg). Then co-processing agents viz. urea (1000 mg), glycerin (1 ml) and propylene glycol (1 ml) were triturated properly in geometric progression with the above solution. Then, it was further subjected to magnetic stirring for 45 min. The bionanogels thus obtained was placed in well-closed container and stored in the refrigerator for further use. The formulations prepared for bionanogels using *C. verum* and guargum are given in Table 1 and 2.

Table 1. Formulations of aripiprazole-loaded bionanogels using *C. verum.*

Formulation	FC1 (1:.1)	FC2 (1:.2)	FC3 (1:.4)	FC4 (1:.6)	FC5 (1:.8)	FC6 (1:1)	FC7 (1:1.5)	FC8 (1:2)	FC9 (1:4)	FC10 (1:6)	FC11 (1:10)
Aripiprazole (mg)	10	10	10	10	10	10	10	10	10	10	10
Bio-retardent/ Bio-stabilizer - *C. verum* (mg)	10	20	40	60	80	100	150	200	400	600	1000
Gelling agent - 1. Sodium alginate (mg)	100	100	100	100	100	100	100	100	100	100	100
2. HPMC (mg)	100	100	100	100	100	100	100	100	100	100	100
3. PVA (mg)	100	100	100	100	100	100	100	100	100	100	100
Co-processing agent 1. Glycerine (ml)	1	1	1	1	1	1	1	1	1	1	1
2. Propylene glycol (ml)	1	1	1	1	1	1	1	1	1	1	1
3. Urea (mg)	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
Distilled water (ml)	10	10	10	10	10	10	10	10	10	10	10

Table 2. Formulation of aripiprazole-loaded bionanogel using guargum (synthetic polymer).

Formulation	**FU1 (1:1.5)**	**FU2 (1:2)**	**FU3 (1:4)**
Aripiprazole (mg)	10	10	10
Bio-retardent/ Bio-stabilizer - guargum (mg)	150	200	400
Gelling agent - 1. Sodium alginate (mg)	100	100	100
2. HPMC (mg)	100	100	100
3. PVA (mg)	100	100	100
Co-processing agent - 1. Glycerine (ml)	1	1	1
2. Propylene glycol (ml)	1	1	1
3. Urea (mg)	1000	1000	1000
Distilled water (ml)	10	10	10

Evaluation of the formulated Aripiprazole loaded bionanogel

The aripiprazole-loaded bionanogels were evaluated for various parameters such as pH, texture, spreadability, % entrapment efficacy, nano-size distribution and in vitro release study.

pH Measurement

The pH of formulated bionanogels was determined by pH meter (manufacturer). The pH meter was first of all calibrated using potassium chloride solution. Thereafter, the electrode is first dipped in the distilled water and then the pH of bionanogels was determined.

Texture

The texture of the formulated bionanogels was determined by applying the bionanogels on the skin and the results were reported.

Spreadability

The bionanogels (each 0.1 ml) were taken and kept over a glass plate. Then another glass plate was kept over it. The area covered by the bionanogels after 5 min was measured.

% Entrapment efficacy

The entrapment efficacy was determined in bionanogels, a weighed amount (10 mg) of each aripiprazole-loaded bionanogel was suspended into 10 ml of distilled water. The resultant solution was filtered through 0.45 mm Whatman filter paper. This solution was assayed for drug content by UV-Vis spectrometer at λ_{max} 261 nm and the corresponding absorbance was recorded. The entrapment efficacy was calculated according to the following formula:

Entrapment efficacy = [(Actual drug content/ Theoretical drug content)*100]

Preliminary determination of nanosize distribution

The bionanogel (10 mg) was dispersed in 10 ml of distilled water. The resultant solutions were filtered through 0.45mm Whatman filter paper. These solutions were then subjected for determination of % transmittance at 200 nm to 800 nm, respectively using Shimadzu UV-Vis spectrophotometer-1800.

In vitro drug release

M S diffusion cell : The in vitro drug diffusion was carried out in M S diffusion apparatus. This was a static method and employed complete replacement of the sample. The aripiprazole-loaded bionanogels (1 ml) was kept in the donor compartment and the receiver compartment was filled with 13 ml of buffer. The complete sample was withdrawn after 30 min and the receiver compartment was refilled with 13 ml of fresh buffer. The samples were withdrawn at regular time intervals for 24 h. The amount of drug release was assessed by measuring the absorbance at 261 nm using UV-Vis spectrophotometer.

Franz diffusion cell : The Franz diffusion cell was used for studying the in vitro release. The dialysis membrane was tied to the terminal portion of the cylindrical donor compartment. Aripiprazole-loaded bionanogels (1 ml) were placed in donor compartment of Franz diffusion cell. The receptor compartment contained 7 ml of buffer solution of pH 7.4 maintained at 37 °C under mild agitation using magnetic stirrer. At specific time intervals, samples of 3 ml were withdrawn and immediately restored with the same volume of fresh phosphate buffer. The amount of drug released was assessed by measuring the absorbance at 261 nm using UV-Vis spectrophotometer.

Stability studies

The stability studies were conducted as per ICH guidelines. The stability testing of the pharmaceutical product is done to ensure the efficacy, safety and quality of active drug substance and dosage forms and shelf life or expiration period. The stability studies of the formulations were conducted at 40±2 °C, 25±2 °C and 2±5 °C

temperature values, respectively. After every 15 days, the aggregation, nature, colour change, and in vitro drug release of formulations were determined.

RESULTS AND DISCUSSION

Isolation of the biomaterial

The biopolymer was isolated from by simplified economic process. The optimisation of biopolymer isolation process was repeated six times for and the % yield was calculated. During optimisation, the results obtained were reproducible with insignificant variation and can be adapted for scaling up in bulk manner. The % yield for biomaterial from the bark of *C. verum* was found to be 5% w/w.

Physicochemical properties biomaterial

The biomaterial obtained from the bark of *C. verum* was obtained in powdered texture that was dark brown in colour with characteristic odour, bitter in taste and solubility was reported in chloroform, methanol and water. The biopolymer confirmed the presence of carbohydrates and reducing sugar and absence of protein and starch.

Drug excipient interaction studies

After performing the UV method shows λ_{max} of drug-excipient mixture near about pure drug. So, drug-excipient interaction study showed that there was no interaction between drug and biomaterial, and biomaterial was compatible with the drug. As no any interaction was found, so it indicates that the biomaterial was found useful in formulation of bionanogels (Fig. 1).

Preparation of calibration curve of drug

The calibration curve of aripiprazole was prepared with phosphate buffer pH 7.4, 4.7 and methanol. The standard curve of the drug was prepared with pH 7.4, 4.7, different media, methanol, and showed linearity. The line slope was found to 0.0546, 0.0734, 0.0147 and R^2 values to 0.9187, 0.9881, and 0.9715, respectively.

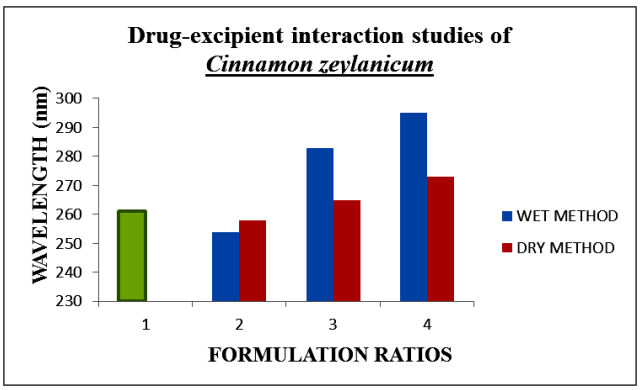

Fig. 1. Interaction studies of drug and biomaterial from *C. verum* by wet and dry methods.

Spectral studies

The result of IR spectrum of biomaterial isolated from the bark of *C. verum* exhibited the important signals at 3157 cm^{-1}, 3142 cm^{-1}, 1408 cm^{-1}, 1392 cm^{-1} and 875 cm^{-1} which clearly indicated the presence of hydroxyl, ketonic, sulphonyl, methyl and amine groups in biomaterial (Fig. 2).

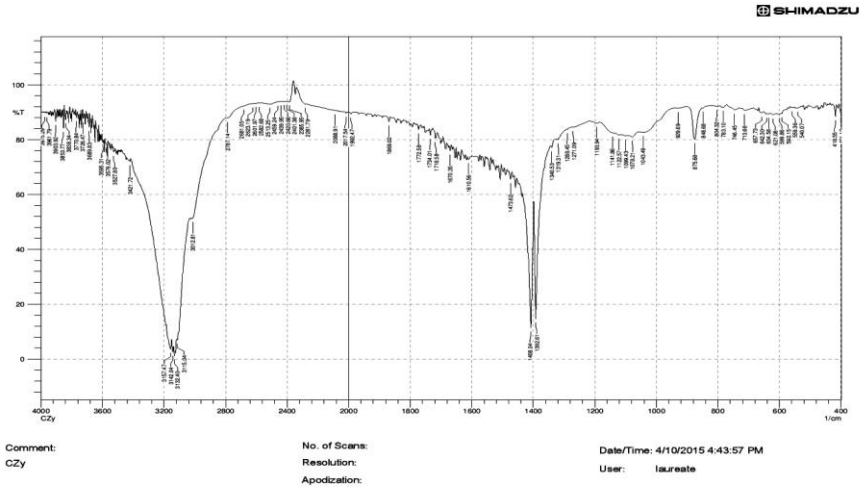

Fig. 2. IR Spectrum of *C. verum* biomaterial.

Evaluation of aripiprazole bionanogels

pH Measurement

The pH values of the aripiprazole-loaded bio-nanogels prepared using biomaterial isolated from the bark of *C. verum* (FC1-FC4) were found in the range of 7.2 to 8.1. The pH values of the aripiprazole-loaded bionanogels prepared using standard polymer guargum (FG1-FG2) were found in the range of 7.8 to 8.0. The graphical representation of the pH values is given in Fig. 3.

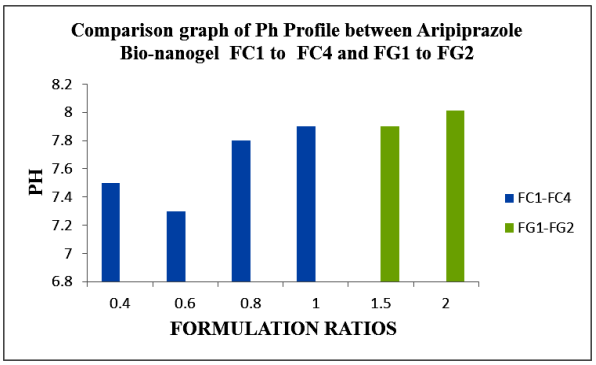

Fig. 3. Comparision graph of pH profile between aripiprazole bionanogels FC1- FC4 and FG1-FG2.

Texture

All the formulated aripiprazole loaded bionanogels [FC1-FC4, FG1-FG2] were found to have a smooth texture on the application on skin.

Spreadability

The spreadability of the aripiprazole loaded bionanogels prepared using biomaterial isolated from the bark of *C. verum* (FC1-FC4) was found in the range of 5.3 to 7.3 cm. The spreadability values of the aripiprazole-loaded bionanogels prepared using standard polymer guargum (FG1-FG2) were found in the range of 3.5 to 3.9 cm (Fig. 4).

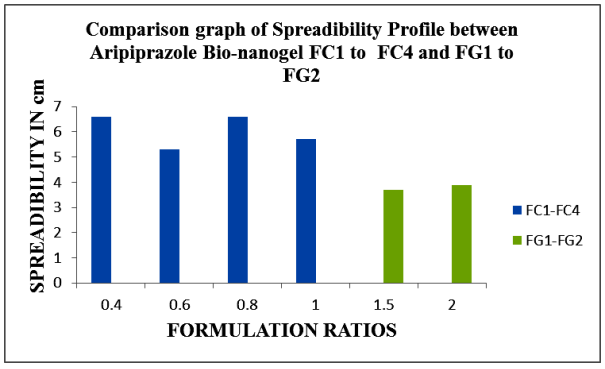

Fig. 4. Comparison graph of spreadability profile between aripiprazole bionanogels FC1-FC4 and FG1-FG2.

% Entrapment efficacy

The entrapment efficacy of the Aripiprazole loaded bionanogels prepared using biomaterial isolated from the bark of *C. verum* (FC1-FC4) was found in the range of 71%-95%. The entrapment efficacy of the Aripiprazole loaded bionanogels prepared using standard polymer Guargum (FG1-FG3) were found in the range of 75%-77% (Fig. 5).

Determination of nanosize distribution

The preliminary size distribution of bionanogels (FC1-FC4 and FG1-FG2) were done by the determination of % transmittance using UV-VIS spectrophotometer (shimadzu-1800) which gave a preliminary idea about the size distribution of particles as smaller the particle more was the % transmittance and vice versa (Fig. 6 and Fig. 7).

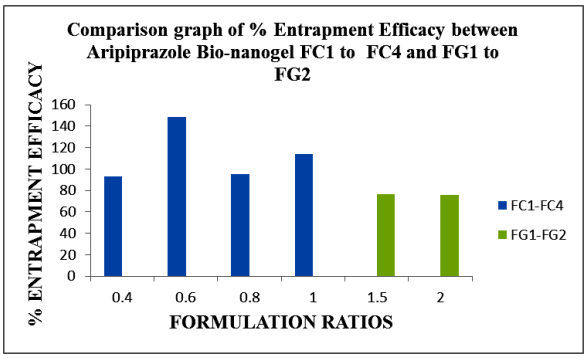

Fig. 5. Comparison graph of % entrapment efficacy between aripiprazole bionanogels FC1-FC4 and FG1-FG2.

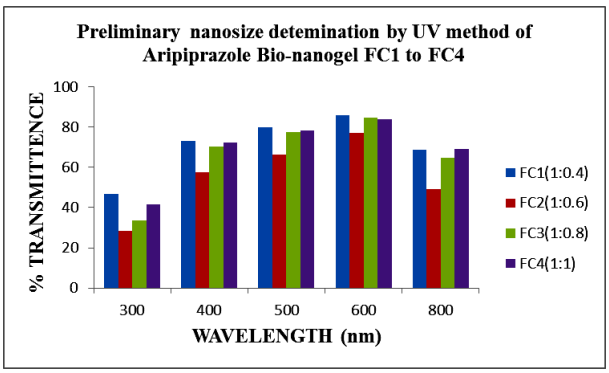

Fig. 6. Preliminary nanosize detemination of aripiprazole bionanogels FC1-FC4.

In vitro drug release of aripiprazole-loaded bionanogels

In vitro permeation studies were performed for all the formulations. The mechanism of aripiprazole released from the bionanogels was studied by fitting the release data in different kinetic models such as Zero order, First order, Higuchi Matrix, Peppas Korsmeyer and Hixson-Crowell and determining the R^2 values of the release profile corresponding to each model. Its % drug release, T50% and T80% were calculated and based on other parameters were arranged in decreased manner.

The drug release pattern for formulations FC1-FC4 containing biomaterial isolated from bark of *C. verum* based on the T50% and T80% was found to be FC3 (0.8%) > FC4 (1%) > FC2 (0.6%) > FC1 (0.4%). In vitro drug release was performed for all the formulations and the data indicate that drug-loaded formulations show the sustained release behaviour.

The graph was plotted between % DR and time, the R^2 value, T50% and T80% were calculated from the graph, the FC3 (0.8%) formulation was found to be the best formulation showing an R^2

value of 0.9831, T50% of 51 h and T80% of 72 h, respectively. According to the release kinetics, the best fit model was found to be Peppas Korsmeyer with Fickian Diffusion (Higuchi Matrix) as the mechanism of drug release.

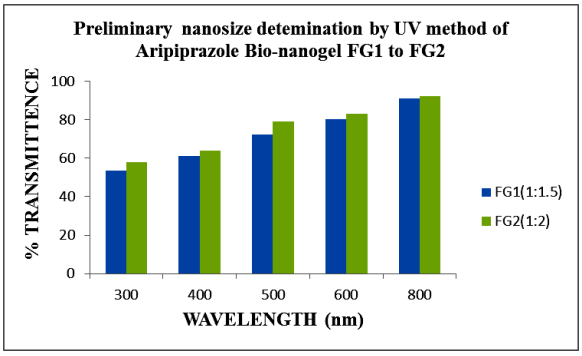

Fig. 7. Preliminary nanosize detemination of aripiprazole bionanogels FG1 to FG2

The drug release pattern for formulations FG1-FG2 containing standard polymer Guar Gum based on the T50% and T80% was found to be FG1 (1.5%) > FG2 (2%). In vitro drug release was performed for all the formulations and the data indicate that drug-loaded formulations show the sustained release behaviour.

The graph was plotted between % CDR and time, the R^2 value, T50% and T80% were calculated from the graph, the FG1 (1.5%) formulation was found to be the best formulation showing an R^2 value of 0.9899, T50% of 16.9 h and T80% of 39.5 h, respectively.

According to the release kinetics, the best fit model was found to be Peppas Korsmeyer with Fickian Diffusion (Higuchi Matrix) as the mechanism of drug release. On comparing all the parameters, the formulation FC3 (0.8%) of *C. verum* and FG2 (1.5%) of Guar Gum were found to be the best formulations as it showed better permeation and less T50% and T80% in less concentration of bio polymer among all the formulations. The drug release pattern for the best formulations among all the formulations based on the T50% and T80% was found to be FC3 (0.8%) > FG2 (1.5%).

Table 3. T50% and T80% values of aripiprazole bionanogels using *C. verum* biopolymer.

***C. verum* (Ratio)**	**T50% (h)**	**T80% (h)**
FC3 (1:0.4)	15.2	35.3
FC4 (1:0.6)	17.3	40.3
FC5 (1:0.8)	51	72
FC6 (1:1)	25.8	60

Table 4. T50% and T80% values of aripiprazole bionanogel using guargum (synthetic polymer).

Guargum (ratio)	**T50% (h)**	**T80% (h)**
FG1 (1:1.5)	16.9	39.5
FG2 (1:2)	13.9	32.3

Table 5. Kinetic release of aripiprazole bionanogel using *C. verum.*

Formulation	**R^2**					**Best fit model**	**Mechanism of action**
	Zero order	**First order**	**Higuchi matrix**	**Peppas**	**Hixson crowell**		
FC3 (1:0.4)	0.9252	0.9708	0.9266	0.9869	0.9631	Peppas Korsmeyer	Anomalous transport
FC4 (1:0.6)	0.8640	0.9469	0.9081	0.9764	0.9258	Peppas Korsmeyer	Fickian diffusion (Higuchi matrix)
FC5 (1:0.8)	0.8354	0.8738	0.9199	0.9831	0.8614	Peppas Korsmeyer	Fickian diffusion (Higuchi matrix)
FC6 (1:1)	0.7836	0.8579	0.9209	0.9834	0.8344	Peppas Korsmeyer	Fickian diffusion (Higuchi matrix)

Stability studies

The formulations were observed after every 7 days for 1 months and no significant change was observed in physical appearance (i.e. colour and odour) of the Aripiprazole-loaded bionanogels. All the formulations remained stable in all the storage conditions. Thus, on the basis of the present study, it can be confirmed that the prepared aripiprazole-loaded bionanogels are stable in different conditions, and these can be considered for a suitable drug delivery.

Table 6. Kinetic release of aripiprazole bionanogel using guargum.

Formulation	**R^2**					**Best fit model**	**Mechanism of action**
	Zero order	**First order**	**Higuchi matrix**	**Peppas**	**Hixson crowell**		
FG1 (1:1.5)	0.8826	0.9562	0.9151	0.9899	0.9363	Peppas Korsmeyer	Fickian Diffusion (Higuchi Matrix)
FG2 (1:2)	0.8915	0.9693	0.9225	0.9807	0.9497	Peppas Korsmeyer	Anomalous Transport

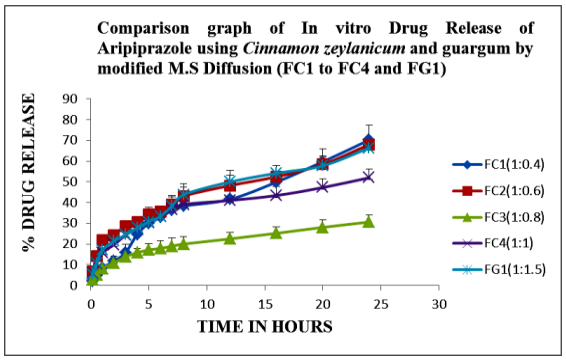

Fig. 8. Comparison graph of in vitro drug release of aripiprazole using *C. verum* and guargum (FC1-FC4 and FG1).

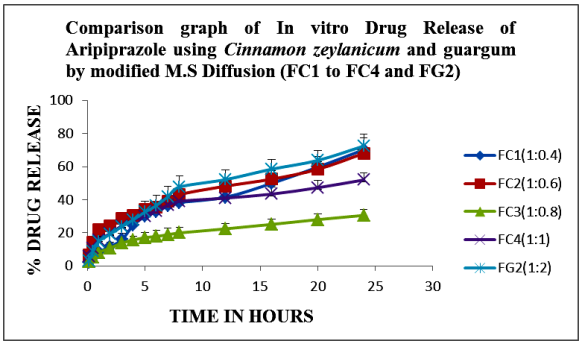

Fig. 9. Comparison graph of in vitro drug release of aripiprazole using *C. verum* and guargum (FC1-FC4 and FG2).

CONCLUSION AND FUTURE PERSPECTIVES

The current research work enlightens the novelistic approach for transcranial delivery specificity of API which can be achieved by designing an effective nanosized aripiprazole loaded bionanogels. In this research work, an effort was made to isolate a novel biopolymer from various edible sources and screened its inbuilt retardability. These biopolymers are used as bio-stabilizer and bio-retardant for designing the formulation.

All the formulations were evaluated for its in-vitro evaluation parameter including pharmacokinetic and pharmacodynamics parameters. In this study, insignificant amount of drug was noticed in the blood which indicates that majority of the drugs might have been reached to the brain via neural pathway mechanism.

Apart from this, the novelistic trans-cranial platform can be used to deliver APIs for both systemic and local delivery by suitably designing formulations like nanogels, hydrogels, bionanogels, in-situ nanogels, flexi films, bioniosome, proniosome, transferosome, desmosomes, cubosomes, liposome, solid-lipid nanoparticle, and colloidal gels.

The formulated aripiprazole-loaded bio-nanogels needs further preclinical studies for exploring the scientific data by administering the formulation over a forehead region of animals in ordered to target the Aripiprazole in brain region via meninges, emissary veins. Thus, formulation needs to further studies, pharmacodynamics and clinical studies. So that product can be launched in the market for the better therapeutic compliance and minimising the adverse reaction of aripiprazole.

In this research work, the potential of nanosized aripiprazole loaded bionanogel for transcranial delivery is investigated bionanogels for trans-cranial use have several favourable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf-life, bio-friendly and pleasing appearance. These bionanogels are having major advantages on novel vesicular systems as well as on conventional systems in various aspects. Bionanogels are a relatively newer class of dosage form created by entrapment of a large amount of aqueous or hydro-alcoholic liquid in a network of colloidal solid particles. The bionanogel formulations generally provide faster drug release compared with ointment and creams.

The biopolymer is used to prepare bionanogels because of its biodegradability, biocompatibility, non-toxic, non- irritant in nature and no reaction on applying on the skin. Physicochemical characterization of biopolymers such as colour, odour, taste, texture and chemical tests were carried out. These isolated biomaterials are rich in protein, fibres and carbohydrates. Biopolymer was found non-toxic in nature, so these are suitable for preparing bionanogels for transcranial drug delivery. These biopolymers were devoid of irritancy to cranium surface because of its inertness, so these biopolymers were selected for formulating aripiprazole bionanogels.

Bionanogels were prepared by emulsion polymerization method which is the easiest and reproducible method to prepare bionanogels without the need of any sophisticated instruments. Drug to polymer ratio was chosen at four levels for the bark of *C. verum* FC1 (0.4%), FC2 (0.6%), FC3 (0.8%), FC4 (1%) and two levels for standard polymer guargum FG1 (1.5%), FG2 (2%).

On the basis of evaluations parameters, FC5 (0.8%) of *C. verum* and FG1 (1.5%) of guargum were selected as the best formulations.

Short term stability study revealed stable bionanogel with no significant change in physical appearance and pH was found stable. This novelistic work was scientifically proven by suitably nanosized active pharmaceutical ingredient and, its pharmacological action, the significant action was produced. Efficient efforts are made in this research work for approach this novel route by formulated aripiprazole bionanogel for trans-cranial delivery for meningitis likewise to reduce its adverse action. During this process, biomaterial was isolated and characterised for

formulation in order to achieved controlled release for prolonged period of time.

The conclusion was drawn that the isolated bio-polymer obtained from the bark of *C. verum* is bio-compatible, bio-degradable due to its edible nature. The bio-polymer showed its inbuilt drug retardability and to provide prolonged drug release from the formulation at FC3 (1:0.8) concentration. When the nanoparticles are incorporated into the optimised bionanogel then these unique formulation can be used for targeting Aripiprazole to the brain by administering a drug through transcranial via frontal skin. The drug may reach to the brain as this area is enriched with emissary veins and neurones. Hence the conclusion was drawn that optimised formulation is significantly feasible to deliver aripiprazole to the brain via the transcranial route.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

Kabanov AV, Vinogradov SV (2008). Nanogels as pharmaceutical carriers. In: *Multifunctional pharmaceutical nanocarriers*, Torchilin V (Ed.). Springer Science, New York, Vol 14, pp. 67-80.

Kamila SN, Satheesh Madhav NV, Sarkar CN (2014). Evaluation of effective Medhya formulation on trans-cranial treatment on rat. International Journal of Biomedical Research, 5, 427-31.

Kamila SN, Satheesh Madhav NV, Sarkar CN (2015). Amnesic potentiality of diazepam at low dose on administration via transcranial route in rodents. International Journal of Pharmaceutical Sciences and Research, 6, 300-07.

Mohanraj VJ, Chen Y (2006). Nanoparticles – A Review. Tropical Journal of Pharmaceutical Research, 5, 561-73.

Pathirana W, Kariyawasam SH, Tibbotumunwa H, Perera K (2006). Brain targeted transcranial route of drug delivery of diazepam. Indian Journal of Pharmaceutical Sciences, 68, 493-6.

Seeman P (2002). Atypical antipsychotics: mechanism of action. Canadian Journal Psychiatry, 47, 27-38.

Uzun S, Kozumplik O, Mimica N, Folnegović-Smalc V (2005). Aripiprazole: an overview of a novel antipsychotic. Psychiatria Danubina, 17, 67-75.

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