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An Overview on Biopolymer: A Novelistic Bio-Excipient in Nanoparticulate Drug Delivery

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Abstract

The point of this review is to feature the novelistic properties as bioexcipient, isolated from different regular natural sources like legumes, seeds, leaves, vegetables, bits, roots, barks and so on and to investigate the probability in medication conveyance framework. The biomaterial s have been exposed to different physicochemical assessments alongside unearthly examination including UV, FT-IR, Mass and 1H NMR. The confined biomaterial was discovered tom be polymeric in nature having a various utilitarian properties. Based on its inbuilt polymeric properties, the biomaterial secluded from various sources, can be utilized as an option in contrast to accessible standard polymers at extremely efficient economical scale. The separated biopolymer comprised of an interesting polymeric properties like accessible standard polymers. The isolated biomaterial from natural sources shown distinctive inbuilt polymeric properties by execution of various physico-substance examination. As we probably are aware there are various polymers accessible and oftentimes utilized design of novel medication. Yet, detached biomaterial from natural sources have demonstrated about their novelistic various properties like biodegradability, bioretardant, bioadhesive, filmability etc.

Keywords: Biopolymer; Biocompatible; Biomaterial; Natural sources; IR; NMR Spectroscopy.

1. Introduction

Biopolymers [1], isolated from natural sources may be used as novel excipients having a polymeric nature. These isolated biopolymers have excellent bioretardant, bio stabilizer, and mucoadhesive properties. It has the excellent film-forming ability, and bio-stability properties [2]. The isolated bio-polymers have excellent drug release rate controlling abilities. Since these are natural and edible, they are biodegradable and may be used as an alternative to standard synthetic and semi-synthetic polymers [3]. The isolated biopolymer shows significant biodegradable, mucoadhesive, filmability, and retardability properties which are similar to properties of synthetic standard polymers [4]. They have most of the novel properties which can be safely used for drug delivery. The biopolymers are isolated from natural sources [5] which are economical. The synthetic polymers are prepared by using the different chemical treatment which has many harmful effects. The biopolymers have unique novel properties [6]. The biopolymers may be used for controlling the drug release in a sustained way, controlled way, extended way, prolonged way and thus are used as drug carrier bioexcipients [7] [7]. Since they are having a natural origin and biodegradable in nature can be sued for minimizing the unwanted effects with synthetic polymers [8-10].

2. Advantages of Novel Biopolymer

1. Biodegradable
2. Biocompatible
3. Excellent bioretardant property
4. Biostabilizer
5. Excellent bioretardant
6. Natural
7. Economical

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8. Environmental friendly
9. Excellent filmability
10. Excellent filmability

3. Bionanoparticles

Bionanoparticles are the nanoparticles that are prepared by using the novel biocompatible and biodegradable biopolymers. We can use the novel polymeric properties in developing the bio-nano particles for targeting the drug to the brain via the blood-brain barrier in an easy way. The bio nanoparticles may release the drug to the target insignificant amount. The bio nanoparticles are stable and their excellent release rate controlling properties makes it novel [11, 12].

4. Novel Sonication method for Nanoparticles Preparation

The bionanosuspension can be prepared by a novel method called the sonication method [13]. In this method, the biopolymer as bio stabilizer cum bioretardant was mixed with other ingredients like a preservative, surface active agent like PVA, nanosizent with the distilled water to make a well-dispersed suspension [14]. Then the mixture was subjected to bath sonication for 10-15 cycles to formulate the nanosized drug-loaded bionanosuspension [4, 15].

5. Evaluation Parameters for Biopolymeric Nanoformulations

A never of evaluation parameters can be performed for the prepared nanosuspension as well as bionanosuspension. The different parameters which should be considered are particle size, particle size distribution, zeta potential, particle morphology [16], dissolution study, stability study, dispersibility,% entrapment efficacy, and in vivo study [6, 13].

The analysis of mean particle size and particle size distribution is an important parameter that defines the stability of the bionanosuspension. Nowadays the particle size and stability parameters can be evaluated by the Malvern zeta sizer. The zeta particle size gives an idea about the particle size and a particle size distribution gives an idea about the state of dispersed particle size, any agglomeration, precipitation or any lump is there.

Particle morphology and state of crystallinity is a parameter that gives an idea about for understanding any changes in drug morphology or structure on nanosizing. The amorphous drug-loaded nanoparticles can be characterized in the nanosuspension as well as bionanosuspension. This can be evaluated by x-ray powder extraction, scanning electron microscopy (SEM) characterization, transmission electron microscopy (TEM) characterization. Differential Scanning Calorimetry (DSC) is also another method for characterizing crystallinity [6, 14].

Zeta potential measurement is another parameter for the evaluation of the particle surface charge which defines the stability of the nanosuspension as well as bionanosuspension. Zetasizer can be used for the measurement of the zeta potential. A minimum of ±30MV is generally required for the stability of nanosuspension.

The stability of nanosuspension or bionanosuspension evaluation is very important for the preparation of well-dispersed bionanosuspension. As the particle size is reduced to the nano range, the surface energy is increased and the increased surface energy may lead to the instability of nanosuspension as well as bionanosuspension. So the uniform particle size distribution leads to the stability of nanosuspension as well as bionanosuspension [17].

6. Advantages of Biopolymeric Bionanoformulations Over other Formulations

1. Improved stability of bionanosuspension because of inbuilt properties of biopolymers
2. Maximum drug entrapment efficacy can be obtained by designing bionanosuspension
3. Biocompatible
4. Biostabilizing activity
5. Desired nanoparticles size can be prepared to cross BBB
6. Suitable for brain targeting through ear route administration
7. Enhanced bioavailability
8. Drug may be released in a retardant manner
9. Dose reduction to many folds because of longer residence
10. Enhanced solubility of the drug
11. Reduction of systemic toxicity
12. Biodegradable

6.1. Limitations of Bionanoformulations

1. Stability is a big challenge for the nanosuspension for long-term storage.
2. Storage at a specified temperature.
2. Rate of sedimentation of particles during long term storage.
4. Precipitation issues during storage
5. Accurate dose administration in form of nanosuspension.

7. Nanoparticles in Drug Delivery

Parveen, *et al.* [18], has suggested about the nanomedicine for targeted drug delivery. A number of the drug delivery approaches are under investigation. One of the approach to deliver the drug, recombinant proteins vaccines is nanoparticles. By using the nana particulate systems the kinetic, body distribution profile can be modified [18]. The different polymeric NPs, ceramic NPs, and magnetic NPs, polymeric micelles and dendrites can be used for the drug targeting. Mohanraj and Chen [19], have mentioned about nanoparticles. His can be prepared by capsulating the drug in polymeric membrane [19]. A number of nanoparticulate systems like nanoparticles, nanospheres can be prepared drug targeting. In matrixes system the drug is physically and uniformly disperse in polymer matrix. This is called nanospheres. The hydrophilic polymer like Polyethylene glycol has been used as the drug delivery devices which circulated for long time and also target the desired cells, organs. Reis, *et al.* [20] stated about the different nanoencapsulation methods [20]. In this way the polymeric nanoparticles may be prepared by using the polymers which show hw biocompatibility, effective drug release, and sustained release. A number of method like polymerization method. Thus the drug may be encapsulated in nano capsules and can be used for the targeting of drug to the target sites. It was also described about the development of camptothecin-loaded SLN and characterized of the different properties like particle size. The particle size was found to be less than 200nm. These were found to be in homogeneous size distribution with high encapsulation efficiencies that is more than 90%. It showed a prolonged release profile of camptothecin from SLN [21]. The Fluorescently labeled nanoparticles were estimated after intravenous administration in in-vivo studies. Blasi, *et al.* [21], described about the formulation of lipid nanoparticles. These were targeted to brain with the aid of computer generated experimental design. The high pressure homogenization was done for the formulation of nanoparticles. Lastly these were found to be suitable for intravenous infusion. These showed the nanoparticles formulation of nano range, which can be suitable as brain targeting carrier. Faraji and Wipf [22], stated about the application of Nanotechnology in various fields specially in drug delivery [22]. They suggested that this field is rapidly growing in developing the nanoparticles with the size of 5–200nm. The nanotechnology can be successfully used for the treatment of various CNS disorders. Patel, *et al.* [23] reviewed about major advances in drug delivery system [23]. Blood brain barrier impedes the passage of drugs which are administered to patients systemically. Brain extracellular matrix minimizes the distribution of drugs. To solve these problems polymeric nanoparticles can be used as a promising solution. To design the carrier for targeting to brain it necessary to understand the composition of blood brain barrier. Thus it is very challenging to design the specific carrier system like design of nanoparticulated system which can easily cross the blood brain barrier. Veiseh, *et al.* [24], presented in their review article about the various design parameters that affect the development of magnetic nanoparticles. MNPs are non invasive agents and used for passive targeting of drugs to organs as well as for disease treatment if therapeutic payload is integrated into magnetic nanoparticles .Authors have also stated that for the evaluation of MNPs and their behavior in body there is need of improved characterization tools [24].

7.1. Biopolymers a Novel Bioretardant in Nanoformulations Development

Madhav [25], stated that a novel biopolymeric material can be used to prepare drug loaded biomicrodwarfs from Arachis hypogea seeds. The goal was to produce a product with a significant processing advantage which satisfies pharmaceutical formulators in scale-up processes. The biopolymer was isolated and characterized for its capability and efficacy to control the release of the drug [25].

Gupta and Madhav [26], have reported a method for isolation of a novel biodispersant from the seeds of Cicero arietinum and formulation of Escitalopram granules containing bio-dispersant. Bio-dispersant was isolated by the treatment the extract from seeds of Cicer arietinum with double distilled water and with ethanol and the bio-dispersant was collected and further analyzed for physicochemical properties like color, odor, particle size, shape, solubility and IR spectral studies. The preparation of Escitalopram, granules were done using drug, lactose, bio-dispersant, bio-binder and other processing agents. We have prepared six different formulations with varying bio-dispersant concentration and bio-binder concentrations [26]. Tangri et. al., (2012) detailed about a method for the formulation and evaluation of sustained release tablets of atorvastatin by utilizing the biomaterial as a novel binder for the formulation of tablets. For the isolation of biomaterial unripe fruit pulp of Artocarpus heterophyllus was taken and the process of isolation used was simplified economic process. The extracted biomaterial was subjected for various physical and chemical parameters like color, color changing point, chemical tests, and I.R. spectral study. Various formulation additives were used to prepare Ibuprofen sustained-release tablets. The three atorvastatin-loaded formulations (FA1-FA3) were prepared by using different drug-polymer ratios of 1:1, 1:3, 1:5, and other excipients like starch, talc, and lactose as diluents [27]. Erasmus and Taylor [28], reported that the cereal grains can also be used as an agricultural raw material rich in several biopolymers. Cereal grains contain major biopolymers like starch, protein, non-starch polysaccharides and lipids. Dry milling, wet milling or combination of the both can be used for the primary extraction of the biopolymers. Grain is separated into its anatomical components by conventional dry milling. Anatomical components can be enriched in certain biopolymers like endosperm flour consist of approximately 80% starch [28].

Madhav and Tangri [27], described about the novel biomaterial from the unripe fruit pulp of Artocaropus heterophyllus and the evaluation of its bio-emulsifying ability by formulation of escitalopram loaded emulsions. The isolation of biomaterial was done from the unripe fruit pulp of Artocarpus heterophyllus by simple and economic process. It was subjected for various physico-chemical parameters like color, color changing point, different chemical tests, and I.R. spectral study. Four drug loaded emulsions were formulated (AH1-AH4) by using varying ratios of the biomaterial [27]. Escitalopram was used as a model drug for the formulation of emulsions. Evaluation parameters like globule size, pH, effect of centrifugation, viscosity, surface tension, creaming, freezing and thawing

cycles and in-vitro release were conducted on the formulated emulsions. The presence of saturated hydrocarbons, aromatic ring secondary, and tertiary alcohol groups was reported in the IR spectra of the isolated biomaterial. Singh [29] described about the various components involved in pharmaceutical formulation development apart from active pharmaceutical ingredients. In recent years, the core area of research in pharmaceutical drug delivery is the excipient development because of its effect on the formulation designing development and targeted drug delivery process in various ways. Because of its low toxicity, biodegradability, stability and renewable nature biopolymers have become the choice of research as excipients. In this review some of the most common used biopolymers as excipient in pharmaceutical drug delivery systems designing have been discussed. [30] described that in order to know the most suitable matrix polymer, before starting the designing it is very important to know the properties of the available polymers. It was reviewed to give an information of the most suitable property of a range of biodegradable polymer [30]. Since the data are widely scattered over many sources and are very scarce compared to the conventional polymer. Data were presented mostly as ranges as well as in graphs for quick comparison reasons. One specific application, thermoplastic pultrusion with flax as reinforcement has been also studied. Singh and Madhav [31], isolated the biopolymer from Tapoica sago. After isolation it was characterized for different parameters like viscosity,ph, conductivity and other physical characteristics. The biopolymer was also tested for the presence of carbohydrate and proteins. The isolated biopolymer was also analyzed for different spectral analysis like FTIR. The isolated biopolymer was used for the preparation of biogel loaded with curcumin for the dermal delivery. It was concluded that the curcumin loaded biogel can be effectively used for the treatment of the wound by using a novel isolated biopolymer form sago as novel retardant cum stabilizer [31].

7.2. Bionanoformulation in Drug Delivery

Madhav and Raina [15], developed and evaluated duloxetine loaded bionanosuspension. The bionanosuspension was prepared by using the biopolymer isolated form Prunus amygdalus seeds. The biopolymer was characterized for different physico-chemical characterization and different spectral characterization. The biopolymer was isolated by the simple economical extraction process and treatment with propanone and then solicited. The residue was recovered and the dried to get the free flowing powder. The duloxetine loaded bionanosuspension was prepared by the bath sonication method. The prepared bionanosuspension was then evaluated for different parameters like particle size, entrapment efficacy, dispersibility, zeta potential, in-vitro release and in-vitro kinetic study and also in-vivo study for the determination of the amount of duloxetine reached to brain via external acoustic meatus. Madhav and Raina [15], explored the feasibility of external acoustic meatus for targeting of escitalopram bionanosuspension to brain. The research reveals that escitalopram loaded bionanoparticles were found to be targeted to brain via external acoustic meatus administration. The bionanosuspension was prepared by using the biopolymer from Piper nigrum in different ratio. The biopolymer consists of the novel retardant properties to release the drug in sustained manner. The research reveals that Piper nigrum can be safely used for development of bionanosuspension for targeting to brain via external acoustic meatus. Madhav and Raina [15], described about the preparation of duloxetine loaded bionanogel for brain targeting via external acoustic meatus. In the research work the biopolymer was isolated form Tagetes papatule and its ability in developing the duloxetine loaded bionanogel for brain targeting. In findings of research the biopolymer was found to have a novelistic characteristic as polymeric nature in developing the bionanosuspension. The bionanosuspension was found to be suitable for delivering the drug to brain. So the conclusion was that the external acoustic route can be used as the promising route for drug targeting to brain in treatment of depression. [14], describes about formulation of chlorpromazine bio-nanogel by using the isolated biopolymer as bioretardant from Prunus amygdalus. The prepared bionanogel was evaluated for the delivery of chlorpromazine targeting to brain. The nanoparticles were prepared by solvent evaporation method. The formulated bionanogel were evaluated for the t50%, in-vitro release, in-vivo release study, and pharmacokinetic study. FA8 (1:15) was selected as the best formulation. Madhav and Raina [15], researched about the development of nanosized duloxetine via external acoustic meatus. The bionanosuspension was developed by using the biopolymer from the berries of Piper nigrum. The prepared bionanosuspension was evaluated for the different parameters like ph, % transmittance, content uniformity, and in vitro drug release and exvivo study. The obtained results were found to be significant for the treatment of CNS disorder. The drug was found to be targeted to brain in significant amount and this rote was found to be suitable for the delivery of dulexotine and in treatment of depression [15, 17]. Tyagi and Madhav [3] researched about a new novel innovative approach for the development of the fluvoxamine loaded bionanosuspension. The bionanosuspension was prepared by using the isolated biopolymer form the Santalum album. The biopolymer was characterized for in-vitro release, t50%, r^2 values and kinetic study to know drug release mechanism. The results were evaluated for identifying the best fit model in drug release. Thus it was concluded that the isolated biopolymer can be suitably used for the development of stable drug loaded bionanosuspension [27].

7.3. Future Aspects of Biopolymers in Drug Delivery

A number of biopolymers were isolated form diffrerent edible and other natural sources like seeds, fruits and flowers. The different physiso-chemical properties were evaluated like %yield, solubility, particle size, pH, rhelogical properties, SEM, FTIR, Mass, NMR, DSC and Cell line toxicity studies which revealed that the most of the isolated biopolymers were found to be significant % yield, water soluble, with pH as that of similar to physiological pH. The isolated biopolymers were found to be free flowing with their uniform particle size. The SEM image revealed that the most of the biopolymers were found to be granular in nature with flaky appearance which revealed their polymeric nature of the biopolymers [32]. FTIR analysis of biopolymers revealed their polymeric nature because of the presence of different functional group like alcoholic, carboxylic group, ketonic group, amino

group et. Mass and DSC spectral analysis of the isolated biopolymers showed the high molecular weight structure with polymeric nature as the polymers [33]. The isolated biopolymers still have not explored for their novel inbuilt characteristics in drug delivery, can be used as an alternative to standard polymers as these are biodegradable, biocompatible, bioretardant cum biostabilizer in nature. The biopolymers may be isolated in economical ways from the different edible natural sources [34].

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