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GLYSINE ENCAPSULATED NANOPARTICLES OF IBUPROFEN

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ABSTRACT

Ibuprofen is sparingly soluble in water, this poor aqueous solubility would create difficulties in pharmaceutical formulations for oral and parenteral delivery that in turn may lead to variable bioavailability. To overcome some of these drawbacks, we planned to utilize glysine (amino acid) to encapsulate ibuprofen and synthesize nanoparticles for drug release in a controlled manner. Glysine polymer is a biocompatible and being used as the retardant material. This has been extensively studied for encapsulation material and controlled release of drug in pharmaceutical technology. In the present study an attempt has been made to formulate and compare ibuprofen loaded glysine nanoparticles, which may provide prolonged drug delivery in the treatment of inflammatory disorders and decrease the related side-effects.

INTRODUCTION

Controlled drug delivery technology represents one of the frontier areas of science, which involve multidisciplinary scientific approach, contributing to human health care. These delivery system offers numerous advantages compared to conventional dosages forms, which include improved efficacy, reduced toxicity, and improved patient compliance and convenience. Such systems often use macromolecules as carriers for the drug. By doing so, treatments that would not otherwise be possible are now in conventional use. This field of pharmaceutical technology has grown and diversified rapidly in recent years. Understanding the derivation of the methods of controlled release and the range of new polymer can be a barrier to involvement from the nonspecialist of the different dosage forms reported, nanoparticles and microparticles attained much importance, due to a tendency to accumulate in inflamed areas of the body. Nano and microparticles for their attractive properties occupy unique position in drug delivery technology.

The controlled release of drug in show and sustained manner is one of the major challenges in drug delivery system. A large number of research efforts on colon-targeted oral delivery of drugs have been pursued over the last decade. Large intestine has the unique physiological features providing an opportunity to achieve colonic delivery in many ways. One can suggest the use of biodegradable polymers that can suggest use of biodegradable polymers that that can release encapsulated bioactive agents directly in to the colon through degradation by enzymes of gastrointestinal tract.

In particular, nanotechnology has led to the significant progress in a biomedical field such as controlled drug/gene delivery [1,2,] tissue engineering [3,4,] imaging of specific sites and probing of DNA structure [5–7]. Among nanomaterials, nanoparticles have been contributing to the progress in this field. In particular, therapies using nanoparticles have widely been achieved for the treatments of cancer [8], diabetes [9], allergy [10], infection [11] and inflammation [12]. Examples of surface modification of nanoparticles are covalent binding between surface and functional molecules or polymers and layer-by-layer assembly [13]. Although polymeric nanoparticles have the difficulty of scaling up, low drug-loading capacity and wide size distribution, they have attracted increasing attention from chemists, biologists, engineers and pharmaceutical scientists because they provide the

possibility of transporting bioactive compounds to specific tissues, cells and cell compartments [14,15.] Compared to ceramic or metal nanoparticles, polymeric nanoparticles can be fabricated in a wide range of sizes and varieties and can sustain localized drug therapeutic agent for weeks [16]. Generally, the well-defined structure of synthetic polymers exhibit well-defined and fine-tunable degradation kinetic as well as mechanical properties [17]. In comparison, proteins offer several advantages over synthetic polymers as they are metabolizable by digestive enzymes into innocuous peptides whereas synthetic polymers may accumulate in the body above a certain molecular weight and result in toxic degradation products [18]. Similarly to proteins, polysaccharides are also digested by the specific enzyme [19]. As far as prolonging circulation time, polysaccharides have advantages over the synthetic polymers such as poly (ethylene glycol) [20].

MATERIALS AND METHOD

Materials:

Ethanol, drug (ibuprofen), glysine, acetone are used in desolvation method. All other chemicals and solvents were used were of analytical grade unless otherwise stated and used without further purification. Double distilled water was used throughout the study.

Method:

Drug-loaded nanoparticles were prepared by desolvation method using Ethanolic solution. The method of desolvation involves drying a sample in a solution. An example of this involves electro-statically bound particles to dissociate by releasing water in an aqueous solution. Nanoparticles of ibuprofen were prepared by desolvation using ethanol under controlled conditions of temperature and pH. Briefly a solution in water was prepared by dissolving glysine in a temperature controlled water bath at 37 °C. The pH of the resulting solution was adjusted to 7.0 with 0.2 M sodium hydroxide. Nanoparticles were formed when the solvent composition was changed from 100% water to 75 vol % hydro-alcoholic solution, upon gradual addition of ethanol, under continuous stirring conditions. The particles obtained were centrifuged at 16000 rpm for 30 min. The nanoparticles were washed twice with deionized distilled.

- Drug loaded nanoparticleswere prepared by desolvation method.
- 20ml acetone solution containing 20 mg ibuprofen.

- Various concentration of glysine (10, 20, 50, 80, 100, and 150 mg/10ml of ethanol) were dissolved by continuous stirring.
- This glysine solution was added drop by drop to the solution containing drug.

Nanoparticles were prepared and analyzed by (SEM) Scanning Electron Microscopy. For the determination of drug loading and particle size in each batch, the concentration of the drug: polymer was varied but unless otherwise stated all other processing variables were kept constant as shown in table.

TABLE: DIFFERENT PARTICLE SIZE AT DIFFERENT PERCENTAGE OF GLYSINE

% of polymer	Conc. of drug (mg)	Acetone (ml)	Conc. Of polymer (mg)	Ethanol (ml)	Ratio of drug: polymer	Mean size (nm)
0.1	20	20	10	10	2:1	300-350
0.3	20	20	20	10	1:1	150-200
0.5	20	20	50	10	2:5	100-125
0.9	20	20	80	10	1:4	50-75
1.2	20	20	100	10	1:5	Liquification of particle
1.5	20	20	150	10	2:15	Liquification of particle

COMPONENTS OF GLYSINE ENCAPSULATED NANOPARTICLES OF IBUPROFEN

The components of glysine encapsulated ibuprofen-nanoparticles formation are glysine, ibuprofen, acetone, ethanol, and water used as a solvent (double distilled water).

Polymer selected -glysine:

Glysine is a colorless, sweet-testing crystalline solid. It is unique among the proteinogenic amino acids in that it is not chiral. It can fit into hydrophilic or hydrophobic environments, due to its single hydrogen atom side chain. In the present study we selected glysine as a polymer due to the following properties:

- Glysine is a simple amino acid
- It is biodegradable in nature so does not cause any toxicity to human body
- Glysine is biocompatible in nature
- It has capacity to polymerize.

Drug selected- ibuprofen:

It is crystalline, white color, odorless, non-steroidal anti-inflammatory, analgesic, antipyretic drug, has both central and peripheral effect and marketed as motrin. The main adverse reaction occurring with motrin tablet is gastrointestinal complains. Uses of ibuprofen are as follows:

- Motrin tablets are indicated for the relief of the sign and symptoms of rheumatoid arthritis and osteoarthritis.
- Motrin tablets are indicated for the relief of mild to moderate pain.
- Treatment of dysmenorrheals pain.
- Also used in musculosketal disorders, soft tissue injuries, fracture, tooth extraction.

Why glysine encapsulated nanoparticles of ibuprofen

Recently, controlled release has become a very a very useful tool in pharmaceutical area, offering a wide range of actual and perceived advantages to the chronic diseases such as rheumatoid arthritis, osteoarthritis, and musculoskeletal disorders including degenerative joint conditions still demand long-term therapy. Based on these characteristics, the drugs appear to be promising are being routinely called for administration. Unfortunately the drug would lead to patient noncompliance and produce certain side-effect such as nausea, vomiting, and others. These problems tend to be serious for drugs with short biological half-lives because they must be taken more frequently. An alternative method to solve such problems is to find a dosage form capable of releasing the drug slowly in controlled manner. Microencapsulation has been used as one of the method to deliver drug in a controlled manner. Polymeric nanoparticles are good vehicles for the delivery of hydrophobic and hydrophilic drugs, since the drugs are protected from possible degradation.

Advantages nanosized drug

It is assumed that when the size of the drug is reduced it will show following novel properties:

- surface: volume ratio increases
- bioavailability increases

- rapid absorption
- stability increases
- efficacy increases

RESULT AND DISCUSSION

The systematic investigation of the synthesis parameters showed that it is possible to prepare glysine-based nanoparticles with different particle sizes and a narrow size distribution. Temperature and nature of the glysine were the most important synthesis factors. SEM images of glysine encapsulated nanoparticles of ibuprofen demonstrated that **Fig. 1**, this image shows particles encapsulated with 0.1% of glysine and particle mean size is 300-350 nm. **Fig. 2**, this image is of 0.3%of glysine with particle 150-200 nm mean size. **Fig. 3** is of 0.5% of glysine shows various particle range and smaller particles than that of 0.1% and 0.2% of glysine and mean particle size is of 100-125 nm. **Fig. 4**, this image is of 0.9% of glysine, shows the best result i.e. smallest size of nanoparticles is formed in this concentration, Mean size of particle is of 50-70 nm. **Fig. 5**, and **Fig. 6**, these images are of 1.2% and 1.5% glysine, shows rupturing of the polypeptide as the concentration of the polymer to that of drug increases the polymer gets liquefied when high energetic beam of electron falls on it.

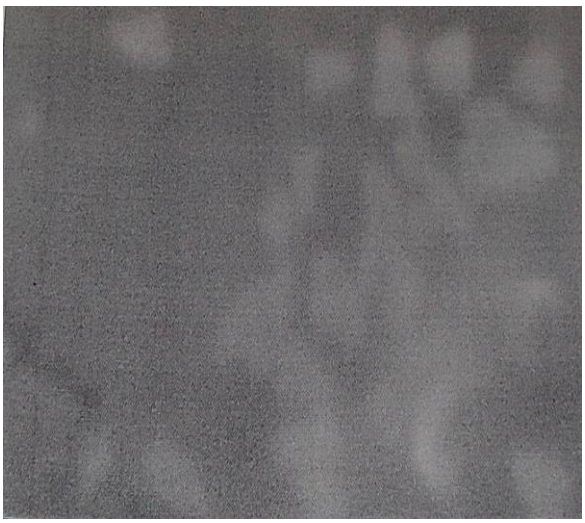

Figure 1: 300-350 nm mean size Nanoparticle

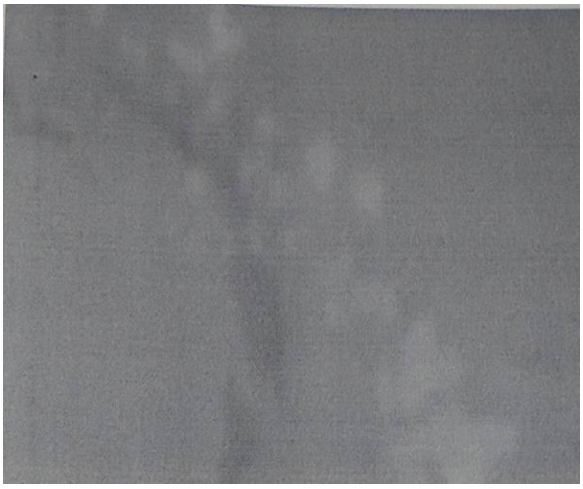

Figure 2: 150-200 nm mean size Nanoparticle

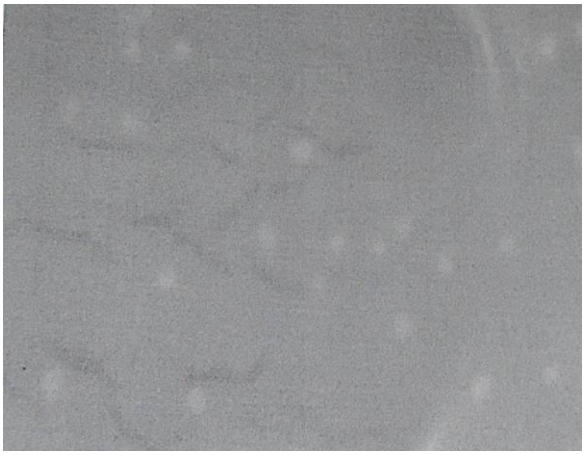

Figure 3: 100-125 nm mean size Nanoparticle

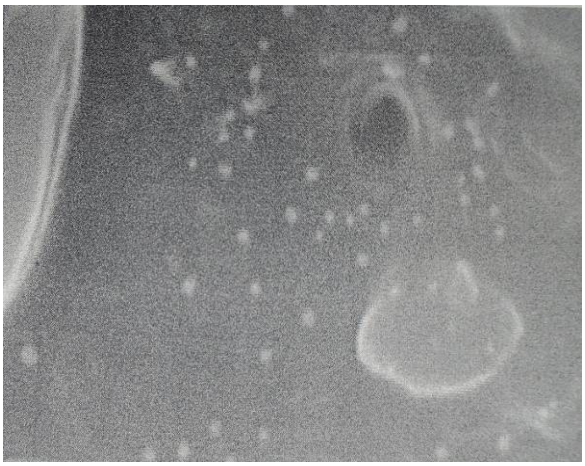

Figure 4: 50-75 nm mean size Nanoparticle

Figure 5: Shows rupturing of the polypeptide

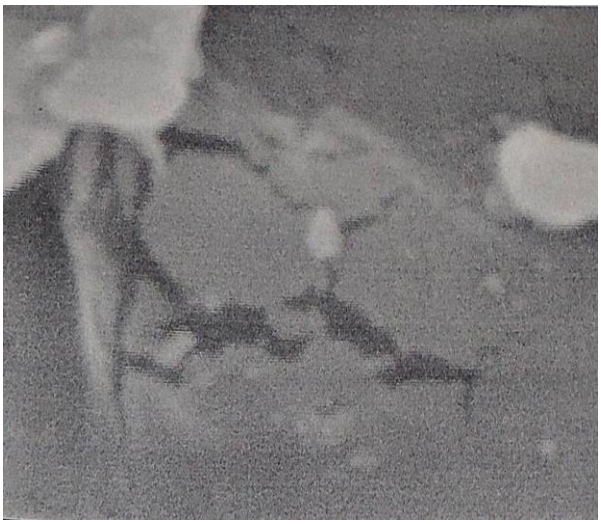

Figure 6: Shows rupturing of the polypeptide

CONCLUSION

Particle size analysis of various concentrations shows optimized formulation at 0.9% of glysine, in which the particle sizes are smaller than that of other concentration. It shows that as the concentration of the polymer increases size of the drug decreases up to some limit and after that the increase in the concentration of the polymer shows rupturing and liquification of the particle, when high energetic beam falls on it.

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