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Preparation and Evaluation of Microparticles Containing Charantin by Solvent Evaporation Technique

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Abstract

The Charantin loaded microparticles were prepared by the solvent evaporation technique by using Eudragit S 100 polymer. Microparticles of different core: coat ratio were formulated and evaluated for process yield, loading efficiency, particle size, zeta potential, in vitro drug release kinetic studies, and stability studies. The microparticles were prepared to have a particle diameter ranging approximately 68-81µm and a zeta potential 85 to 101mV. There was a steady increase in the entrapment efficiency of increasing the polymer concentration in the formulations. The in vitro release for all drug-loaded batches were found to follow to first order and provided sustained release throughout 24 h. No appreciable difference was observed in the drug content of product during 90 days in which microparticles were stored at 4˚C, room temperature, and some little difference found in drug content of product during 90days in which microparticles were stored at an accelerated temperature of 40℃ ± 2℃75% RH. According to the data obtained, these microparticles containing Charantin opens new and exciting perspectives as drug carriers for treating the Diabetes mellitus.

Keywords — *Microparticles, Eudragit S 100, Charantin, solvent evaporation method.*

I. INTRODUCTION

Diabetes mellitus is the commonest endocrine disorder that affects more than 100 million people worldwide (6% population). It is caused by a deficiency or ineffective production of insulin by the pancreas, which results in an increase or decrease in concentrations of glucose in the blood. It can damage many-body systems, particularly blood vessels, eyes, kidneys, heart, and nerves. Diabetes mellitus has been classified into two types, i.e., insulin-dependent diabetes mellitus (Type I) and non-insulin-dependent diabetes mellitus (Type II). Type I diabetes is an autoimmune disease characterized by a local inflammatory reaction in and around islets followed by selective destruction of insulin-secreting cells. In contrast, Type II diabetes is characterized by peripheral insulin resistance and impaired. Allopathic drugs are used to treat diabetes have their side effect & adverse effect like hypoglycemia, nausea, vomiting, hypernatremia, flatulence, diarrhea or constipation, alcohol flush, headache, weight gain, lactic acidosis, pernicious anemia, dyspepsia, dizziness, joint pain. So instead of allopathic drugs, herbal drugs are a great choice, which is having more or less no side effects & adverse effects. Based on the origin's material, Ayurveda medicines are divided into three classes, namely herbal, mineral, and animal. Among this, the herbal formulation has gained great importance and rising global attention recently. Ayurveda has about 700 types of plants listed in its medicinal systems. The use of such herbals is mentioned in the ancient Ayurvedic literature, such as Charaka Samhita and Sushruta Samhita. The discovery of herbals is further complemented with knowledge on the method of isolation, purification, characterization of active ingredients, and type of preparation. The term "herbal drug" determines the part/parts of a plant (leaves, flowers, seeds, roots, barks, stems and etc.) used for preparing medicines. The herbal drugs like Azadirachta indica, Mangifera indica, Ocimum sanctum leaves, Momordica charantia, leaves of Gymnema Sylvestre, the stem of Tinospora cordifolia, the bark of Cinnamomum zeylanicum, rhizome of Curcuma longa, and roots of Withania somnifera are showing antidiabetic activity. Charantin is the main Phytoconstituent present in fruits of Momordica charantia, which is a steroidal glycoside and exists as an equal mixture of stigmasterol glucoside and β-sitosterol glucoside. It has got blood sugar lowering property equivalent to insulin. Charantin at a dose of 50mg/kg shows antidiabetic activity like insulin. Generally, there are so many conventional treatments for treating diabetes mellitus, but they are having own side effects like poor patient compliances and high cost. One of the ways to overcome these problems could be an association with the biodegradable polymeric carriers like microspheres. Microspheres have played a vital role in the development of controlled/sustained release drug delivery systems. Microspheres have been of particular interest from the pharmaceutical point of view, providing the possibility to achieve controlled drug release. Microspheres can be defined as solid spherical particles ranging from 1 to 1000 µm in size. The microspheres are free-flowing powders

consisting of proteins or synthetic polymers, which are biodegradable in nature. Eudragit S 100 possesses some ideal properties of a polymeric carrier for microparticles such as biocompatibility, biodegradability, non-toxicity, and low cost. It exhibits an absorption enhancing effect. Hence, the objective of the work was to formulate microparticles containing charantin by a solvent evaporation method using Eudragit S 100 as a polymer and evaluate its physicochemical characteristics such as particle size, surface morphology, zeta potential, drug loading capacity, and *in vitro* release characteristics.

II. MATERIALS AND METHODS

Charantin used was bought from Shreedha phytochemicals, Jaipur, India, and Eudragit S 100 Rolex chemicals, Mumbai. Polyvinyl alcohol, chloroform were obtained from SD fine chemical ltd, Mumbai, India. All other chemicals used were of analytical grade.

A. Preparation of Microparticles:

Suitable amounts of polymer (Eudragit S 100) were added to a chloroform solution of the drug. The aqueous phase was prepared by dispersing 0.2% PVA (Polyvinyl alcohol) in water. The Drug polymer solution was added to the aqueous phase with constant mixing. The mixture was stirred with a propeller at 500 rpm for 3 hrs at 25^0 for complete removal of chloroform. The mixture was filtered to collect the microspheres, which were then washed with deionized water. These microspheres were dried at room temperature for 24 hrs. (Table 1).

Table No.1: Formulation and physicochemical characterization of Charantin Microparticles

Sl no	Formulation code	Drug and polymer ratio	entrapment efficiency (%)	Particle size (µm)
01	FS1	1:1	81.23%± 0.24	71.55 ±7.05
02	FS2	1:2	84.6%±0. 36	82.35 ±5.24
03	FS3	1:3	92.64%± 0.54	75.68 ±9.51
04	FS4	1:4	87.5%±0. 38	78.49 ±4.6
05	FS5	1:5	88.18%± 0.41	68.98 ±10.8 9

III. CHARACTERIZATION OF PREPARED MICROPARTICLES

A. Fourier transform infrared spectroscopy (FT-IR) analysis: The entire document should be in Times New Roman or Times font. Type 3 fonts must not be used. Other font types may be used if needed for special purposes.

B. B. Practical yield: Freeze-dried microparticles were collected and weighed to determine practical yield (PY) from the following equation 1.

$$PY(\%) = \frac{\text{Microparticles weight} \times 100\%}{\text{Theoretical mass}}$$

The individual values for three replicates were determined, and their mean values are reported.

C. Drug content:

The drug content in each formulation was determined by weighing microparticles equivalent to 30mg of Charantin and dissolving in 100 ml of 7.4 pH phosphate buffer, followed by stirring. The solution was filtered through a 0.45µ membrane filter, diluted suitably, and the absorbance of the resultant solution was measured spectro-photometrically at 281 nm using 7.4 pH phosphate buffers as blank. The drug content of the prepared microparticles was determined by the formula:

$$DC(\%) = \frac{\text{Weight of drug in microparticles} \times 100}{\text{Weight of microparticles}}$$

D. Entrapment efficiency (EE %):

The entrapment efficiency is also known as Association Efficiency. The drug-loaded microparticles were centrifuged at a high speed of 3500-4000 rpm for 30 min, and the supernatant is assayed for non-bound drug concentration by UV spectrophotometer (Das *et al.*, 2005).

Efficiency (DEE) was calculated as follows:

$$DEE\ \% = \frac{\text{Experimental drug content} \times 100}{\text{Theoretical drug content}}$$

E. Scanning Electron Microscopy:

The shape and surface topography of microparticles were examined using Scanning Electron Microscopy (SEM) (JSM-T20. Tokyo, Japan). An appropriate sample of polymeric microparticles was mounted on metal stubs using double-sided adhesive tapes. Samples were gold coated and observed for morphology at an acceleration voltage of 15KV.

F. Particle size distribution:

The size distributions along the volume mean diameters of the suspending particles were measured by dynamic scattering particle size Analyzer (Nanotrac Particle Analyzer 150, Microtrac Inc., PA, USA) (Alexis et al., 2008).

G. In vitro release studies:

In vitro dissolution of all the formulations was conducted by using USP Dissolution apparatus II. Microspheres equivalent to 100 mg of Charantin were taken and placed in the Jar of dissolution apparatus.

The dissolution media used a pH 7.4 buffer solution. The temperature was maintained at 37 ± 0.5°C and rotation was set at 50 pm. 10.0 mL of sample was taken, filtered, and analyzed at 281 nm using a spectrophotometer to get a percentage drug release versus time profile. The fresh medium was replaced for each sample taken out of the apparatus to maintain the sink condition.

H. Kinetic modeling:

To understand the kinetics and mechanism of drug release, the result of *in vitro* drug release study of microparticles were fitted with a various kinetic equation like zero-order (cumulative % release vs. time), first-order (log % drug remaining vs. time), Higuchi's model (cumulative % drug release vs. square root of time), Peppas plot (log of cumulative % drug release vs. log time). R2 and' n' values were calculated for the linear curve obtained by regression analysis of the above plots (Table No.2).

I. Stability study:

The stability study was carried out using the batch FS-3. Formulation FS-3 was divided into 3 sets of samples and stored at 5±3℃ in the refrigerator, room temperature, and 45 ± 2℃, 75% RH in humidity control ovens. After 90 days of drug content of all samples were determined by the method as in drug content, *In vitro* release study of formulation, FS-3 was carried out after 90 days of storage.

IV. RESULTS AND DISCUSSION

i) Physicochemical characterization of microparticles:

Spherical microparticles were formed spontaneously upon addition of the chloroform solution of drug and polymer (Charantin and Eudragit S 100) to the continuous phase polyvinyl alcohol of 0.2% under the stirring with a propeller at 500 rpm. The microparticles are obtained by the solvent evaporation method, which simple process where particles form suspension or emulsion or solution of drug-core with the polymer in an aqueous phase, which is dispersing in chloroform under continuous stirring. The agitation has to maintain, and the solvent evaporates after diffusing through the continuous phase resulting in solid microspheres. The FTIR spectrum shows no significant changes in the drug's chemical integrity and indicates that the polymer and drug are compatible with each other. Microparticles prepared by the solvent evaporation technique were found to be discrete, and through SEM analysis (Fig. 1), their mean size distribution was found to be 72 µm. The drug entrapment efficiency of microparticles containing drug: polymer in various ratios of 1:1, 1:2, 1:3, 1:4 and 1:5 were found to be 81.23%±0.24%, 84.6%±0.36%, 92.64%±0.54%, 87.5%±0.38%, 88.18%±0.41 %(Table 1). Thus there was a steady-state increase in the entrapment efficiency on increasing the polymer concentration in the formulation. Zeta potential of all formulated microparticles was in the range of 85 to 101mV, which indicates that they have excellent stability. (Table 1).

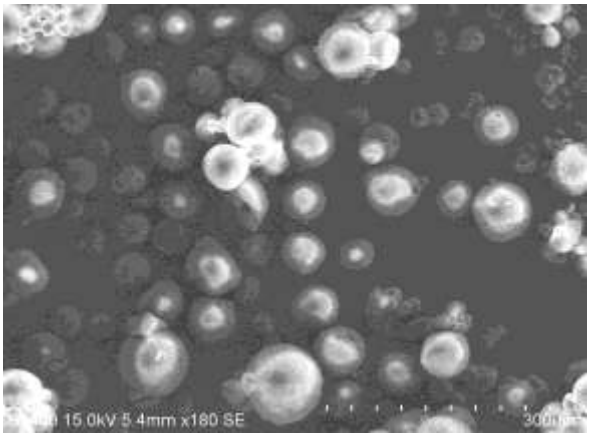

Fig.1: SEM of formulation FS-3

ii) In vitro release of microparticles:

Cumulative percentage drug released for FS-1, FS-2, FS-3, FS-4 and FS-5 after 12 h were found to be 93.09%, 90.32%, 78.01%, 85.08% and 88.60%, respectively(Fig. 2). It was apparent that *in vitro* release of Charantin showed a very rapid initial burst and then followed by a very slow drug release. An initial, fast release suggests that some drug was localized on the surface of the microparticles.

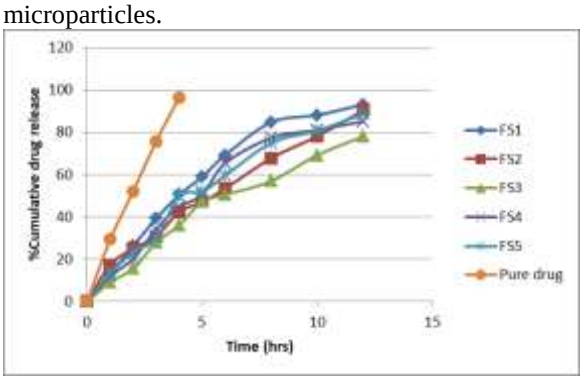

Fig.2: % cumulative drug release of Charantin Microparticles (mean ± SD, n = 3).

iii) Kinetic studies:

The corresponding dissolution data were fitted in various kinetic dissolution models like zero order, first order, and Higuchi, respectively (Table 2), to describe all five formulations' release kinetics. As indicated by higher R_2(coefficient of correlation) values, the drug release from all formulations follows the first-order release and Higuchi model.

Table.2: Correlation coefficients according to different kinetic equations
FS-1, FS-2, FS-3, FS-4, and FS-5 represent formulations 1 to 5, respectively, *etc*.

Since it was confirmed as the Higuchi model, the release mechanism was swelling, and diffusion controlled. The Peppas model is widely used to confirm whether the release mechanism is fickian diffusion, non- Fickian diffusion, or zero-order. '*n'* (release exponent of Korsmeyer-Peppas model) value could be used to characterize different release mechanisms. The 'n' values for all formulations were found to be greater than. This indicates that the release approximates the Non-Fickian diffusion mechanism (13).

iv) *Stability studies:*

The results of the drug content of ideal formulation FS-3 after 90 d of stability testing at different storage conditions were shown in Fig. 3. *In vitro* release profiles for the same formulation stored at different storage, conditions were also shown in Fig. 4.

On comparing this data with the previous data of FS-3, it was observed that there was a slight decrease in drug content when the formulation was stored at 4˚C and Room temperature. Still, there was a significant decrease in drug content when the formulation was stored at 40 ± 2˚C/75% RH because at a higher temperature, there might be a chance for the drug degradation that decreases the drug release.

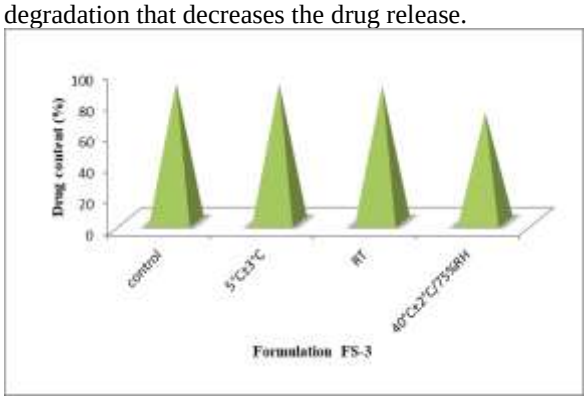

Fig.3: Stability study: comparison of % drug content of formulation FS-3 at 5±3℃, room temperature (29℃) and 40℃± 2℃/75% RH

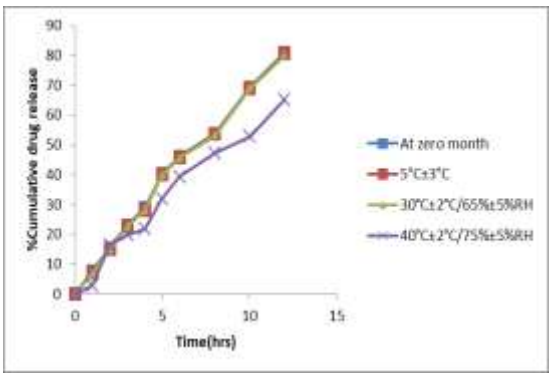

Fig.4: Stability study: comparison of *in vitro* drug release profile for formulation FS-3 at 5± 3℃, room temperature and 40℃± 2℃/75% RH after three months storage.

V. CONCLUSIONS

Charantin microparticles were prepared by the Solvent evaporation method were found to be suitable for controlled release. The microparticles prepared by using Eudragit S 100 as a polymer show prolonged release rate with increasing polymer concentration when compared with other formulations, on the basis of drug content, entrapment efficiency, particle size, surface morphology, zeta potential, and *in nitro* release data's, the FS-3 was selected as an optimum formulation. The stability studies were carried out for the selected formulation FS-3; the results showed that maximum drug content and closet *invitro* release to previous data was found for FS-3 stored at 4˚C, room temperature, and 40℃ ± 2℃/75% RH. Thus the microparticles of Charantin (FS-3) with the core: coat ratio 1:3 was found to be spherical, discrete, and free-flowing and able to sustain/control the drug release effectively.

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