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COMPARATIVE EVALUATION STUDY OF SOLUBILITY ENHANCEMENT FOR BICALUTAMIDE BY SLN AND SOLID DISPERSION METHOD

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ABSTRACT

The present study was carried out to comparative evaluation of solubility enhancement of Bicalutamide. Method for solid lipid nanoparticle preparation is a precipitation method and solid dispersion prepared by the hot plate method. Result expressed as an *in-vitro* release and drug content of Bicalutamide effectively gives by solid lipid nanoparticles than solid dispersion method. So Solid lipid nanoparticle is an effective method for Bicalutamide than solid dispersion.

Keywords*:* - Bicalutamide, Solubility enhancement, Solid-lipid nanoparticle

INTRODUCTION

Among all newly discovered chemical entities that 40% of drugs are lipophilic and fail to reach the market due to their poor aqueous solubility. For orally administered drugs solubility is one of the rate-limiting parameters to achieve their desired concentration in the systemic circulation in pharmacological response[1]. Solid Lipid Nanoparticle is composed of physiological lipid which reduces the risk of acute and chronic toxicity prepared by high-pressure homogenization without the use of organic solvent. They show crystal nature at RT and nanoemulsion at body temperature. Entrapment of bioactive ingredient inside the solidify lipid matrix so SLN prevent the diffusion of bioactive ingredient to the surface of emulsion reduces the incidence of oxidative reaction.[2]

The development of solid dispersions as a practically viable method to enhance the bioavailability of poorly water-soluble drugs overcame the limitations of previous approaches such as salt formation, solubilization by cosolvents, and particle size reduction.[3]

Bicalutamide is a synthetic, nonsteroidal antiandrogen. Bicalutamide competitively binds to cytosolic androgen receptors in target tissues, thereby inhibiting the receptor binding of androgens. This agent does not bind to most mutated forms of androgen receptors. It is an oral non-steroidal anti-androgen for prostate cancer. It binds to the androgen receptor. Bicalutamide competes with androgen for the binding of androgen receptors, consequently blocking the action of androgens of adrenal and testicular origin which stimulate the growth of normal and malignant prostatic tissue.

MATERIALS AND METHODS

All ingredients used were of analytical grade.

METHODS

Preparation of Solid lipid nanoparticles by precipitation method-

For the preparation of nanoparticles, Bicalutamide was dissolved in ethanol and PVP was dissolved in distilled water at RT, Stearic acid was melted separately and adds in drug-containing solution. In drug, lipid mixture adds PVP solution dropwise with the help of injection needle different ratios of the drug, PVP and stearic acid were taken. The mixture

was stirred at RT for 1hr and then slowly evaporated on a boiling water bath. The precipitate as a crystalline powder was obtained and dried in desiccators till free from any traces of organic solvent.[4]

Table No. 1: Formulation Table

Ingredients	S1	S2	S3	S4
Bicalutamide(mg)	100	100	100	100
PVP(mg)	100	100	200	200
Stearic acid(mg)	100	300	100	300

Preparation of Solid dispersion

In the Hot Melt method, carriers were heated at a temperature of 55 ± 0.5ºC and 150 ± 0.5ºC using a thermostatically controlled water bath. Bicalutamide is a 1:1, 1:2, 1:3 and 1:5 Drugs: carrier ratio was dispersed in the melted polymer. The resultant mixture was immediately cooled using an ice-water bath and was maintained for a specific period of 2 hrs. The solidified mass was then removed from the ice water mixture and allowed attaining the room temperature for 24 hrs and then pulverized using a glass mortar and pestle. The pulverized mass was sifted through # 60, weighed and transferred to the glass vials.[5]

EVALUATION

Determination of Percent yield:

The yield of the final solid lipid nanoparticle of all ratios was calculated by using the final weight of solid lipid nanoparticle after drying and the initial wt. of drug and polymer used for the preparation of SLN the following formula is used for calculation of percent yield.

% Yield= Theoretical yield of SLN / Practical yield of SLN ×100

Determination of Drug content:

Powdered SLN and physical mixture equivalent to 10mg Bicalutamide drug accurately weighed and transferred to 100ml volumetric flask about 20ml ethanol added and the flask was shaken gently into dissolving complete residue then makeup volume with ethanol which gives a resulting solution of 100µg/ml. 1 ml of the resulting solution was taken in 10ml

volumetric flask and volume was make up with ethanol the absorbance of this solution was taken at 272 nm In UV spectrophotometry and the drug content was determined.[6]

Determination of solubility:

The solubility of SLN of Bicalutamide was determined in distilled water excess amount of bicalutamide SLN and solid dispersion was added to the 10ml of distilled water in a beaker. These solutions were stirred on magnetic stirred for 4hr. Due to this equilibrium is achieved. Then this solution was centrifuged at 2000rpm for 10min. The supernatant solution was filtered by using watermen filter paper of grade 41 One ml of this filtered solution was taken and diluted with respective medium and absorbance was taken at 272nm.[7]

***In-vitro* Drug release:**

For Solid lipid nanoparticles

In vitro release of Bicalutamide from SLN by using Modified Franz Diffusion Cell performed. For this Dialysis membrane of pore size, 2.4nm was used. The membrane was soaked in double-distilled water for 12hr before mounting on Franz diffusion cell. A volume of 1ml Bicalutamide loaded SLN formulation was placed in the donor compartment and the receptor compartment was filled with 10 ml of dialysis medium containing PH7 buffer solution. 1ml of the sample was withdrawn using micropipette from the receiver compartment within 1hr. of the time interval. The fresh medium was replaced each time to maintain constant medium volume. The sample was analyzed by using UV at 272nm.[7]

For Solid dispersion

A USP apparatus II (paddle apparatus) was used to obtain the *in-vitro* release profile of the drug from all the systems under different dissolution conditions. Dissolution experiments were conducted using three different media (900 ml of water, 900 ml of phosphate buffer, pH 7.4, and 250 ml hydrochloric acid buffer, pH 1.2) at 75 rpm and $37 \pm 0.5°C$. Samples corresponding to 150 mg of Bicalutamide were placed in each vessel. A 5-ml aliquot was withdrawn at regular time intervals and replaced with an equal volume (5 ml) of dissolution media. Samples were filtered through Acrodisc syringe filters (0.45 μm) and assayed using a UV spectrophotometer at 283 nm.[8,9]

RESULTS AND DISCUSSION

Table No. 2: Percent practical yield

Sr. No.	Batch Code	%Practical Yield (SLN)	%Practical Yield (Solid Dispersion)
1	S1	44	55
2	S2	60	58
3	S3	70	63
4	S4	66.66	68

Table No. 3: Drug content

Sr. No.	Batch Code	%Drug Content (SLN)	%Drug Content (Solid Dispersion)
1	S1	6.7	42
2	S2	20.26	46
3	S3	33	51
4	S4	90	54

Table No. 4: Solubility

Sr. No.	Batch Code	Drug Content(SLN)	Drug Content(Solid Dispersion)
1	Bicalutamide	0.00298	0.00298
2	S1	0.023	0.0190
3	S2	0.036	0.0201
4	S3	0.043	0.0250
5	S4	0.150	0.0275

Table No. 5: *In-vitro* drug release:

Sr. No.	Time (hr)	%Drug Release(SLN)	%Drug Release (Solid Dispersion)
1	1	9.4	30
2	2	17.53	36
3	3	37.81	44
4	4	69.01	52

CONCLUSION

It can be concluded that among four batches S4 shows ideal result due to increased wettability may be due to increased polymer concentration and surface area. In the evaluation study, Solid Lipid Nanoparticles shows better drug release and solubility.

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