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Formulation, Optimization and Evaluation of Self-Emulsifying Drug Delivery System of Diclofenac Sodium Tablets

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Abstract

Self-emulsifying drug delivery system (SEDDS) is a class of formulation through which we are able to formulate BSC class II drug and get good enough bioavailability via oral administration. SEDDS is a self-explanatory word, which indicate that a system which convert into emulsion after conventional application. SEDDS restrain two advantages; one is of solid (stability) and another emulsion (faster adverse penetrability). SEDDS formula of STDS6 SEDDS granules was drug: Tween 20:S pan 20: Olic acid PVPK30: CCS (4:7.25:7.21:2.35:18:2.42:18) and formula for SEDDS tablet was SEDDS Granules (Equivalent to one dose) 25% w/w, Lactose 50% w/w, Starch 10% w/w, Guar Gum 9% w/w, Mg. Stearate 2%w/w and Talcum 4%w/w. Tablets were prepared by direct compression method after 30 min of blending of dry content. Dissolution rate test was studied in USP dissolution test apparatus basket Type I (test condition: 900ml 0.1N HCl buffer medium, 37 ± 2°C at 100 rpm). On the basis of the drug release kinetic the formulation S8 was found as the optimized formulation because it provides us the planned release kinetics i.e. zero order release with correlation coefficient (r2=0.994) in the pattern of controlled release study. The % cumulative drug release of the formulation STDS6 was found 99.66 in 120 minutes and thus it may increase the absorption percentage of therapeutic agent.

Keywords: SEDDS, STDS6, drug delivery.

Introduction

It is well known that only the 8% of new drug having the both high solubility and high permeability. Thus, chemist and the pharmacists should have well knowledge about the solubility and permeability of drug. This will help in various ways like- It will help to overcome the problems which are arises during formulation of pharmaceutical products. The choice of best solvent medium for a drug or combination of drugs. The drugs which belong to class-II having the low solubility and high permeability are suitable candidate for SEDDS formulation. A drug like diclofenac sodium is suitable drug for the formulation of SEDDS. The drugs that's permeability is high but the solubility is low are suitable drug for SEDDS formulation. So, diclofenac sodium elongs to

class-II drug in BCS. By applying SEDDS method the solubility of diclofenac sodium can be increased. SEDDS's role in improving oral absorption: SEDDS can increase the amount of solubilized drug to intestinal fluids which gives good drug absorption. Also, enhancement of drug absorption is due to use of lipid base excipients in the formulation. Lot of mechanisms involved to increase the drug absorption like increasing in Effective drug solubility in lumen, Lymphatic transport of the drug, Enterocyte based drug transport, Retardation of gastric emptying time, Membrane permeability. However, the system which containing co-surfactant, having the aqueous phases and oil phase partitioning which may take place leading to a mechanism known as "diffusion and stranding". In this mechanism the oil is solubilize and leading to migration into the aqueous phase.

Preparation and characterization of granules

The SEDDS of diclofenac sodium can be prepared by melting the surfactant mixture of tween-40 in co-solvents like PEG-600 or span-20 by using oil like soyabean oil. During melting the temperature was 70°C. The molten blend was prepared by using China dish. By using different ratio of ingredients, several formulations were prepared. Then the prepared blend is mixed with the drug until a creamy dispersion was produced. Finally, the blended excipients (CCS, Lactose, and PVPK-30) were mixed physically in different proportions. Creamy dispersion was then mixed thoroughly until a suitable mass was obtained. Then this mass was semi-dry after semi dry it was screening and then sends for full dry. After complete dry it was lubricated and then compressed as tablet.

Granules	Bulk density(gm/cm^3) ± S.D	Tapped density(gm/cm^3) ± S.D	Angle of repose(degree) ± S.D	Carr's compressibility index (%)±S.D	Hausner's ratio±S.D
SDTS1	0.561±0.21	0.708±0.12	29.098±0.21	20.76±0.87	1.26±0.43
SDTS2	0.634±0.53	0.689±0.22	35.415±0.11	5.50±0.63	1.08±0.31
SDTS3	0.737±0.19	0.867±0.22	32.133±0.01	11.704±0.13	1.17±0.65
SDTS4	0.746±0.39	0.856±0.13	31.437±0.21	12.218±0.29	1.23±0.27
SDTS5	0.748±0.21	0.854±0.25	29.427±0.64	13.476±0.67	1.15±0.23
SDTS6	0.765±0.61	0.811±0.16	27.452±0.25	19.85±0.53	1.06±0.21

Table 1: Rheological properties of granules prepared for SEDDS

Angle of repose

The angle of repose is calculated for each granule prepared by "static funnel method". The values determined for formulated granules were ranges between 27.452±0.25to 35.415±0.11o . This digit for angle of repose shows that the formulation showed good flow property. In formulation of SEDDS the additives viz. oil, surfactants, co-surfactants and solvents are used thus its ratio should be limited and balanced manner otherwise the flow-ability slightly decreases as they all possess a typical sticky in their physical nature.

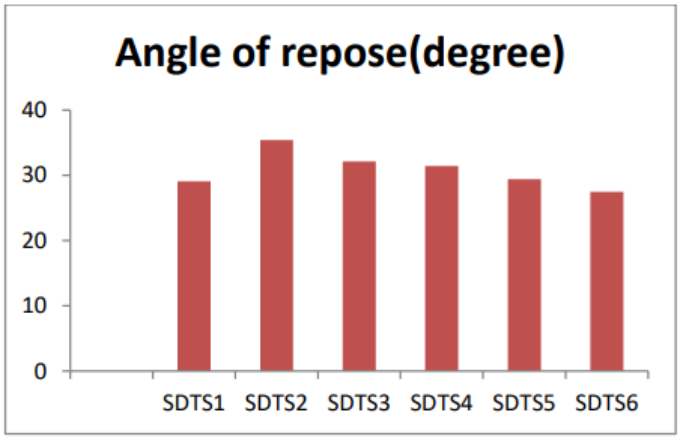

Figure 1: Pictorial presentation of angle of repose Bulk density and tapped density: Bulk density of Formulations was found in between 0.561±0.21 to 0.811±0.16 gm/cm3 and the tapped density of the formulation ranges from 0.689±0.22 to 0.863±0.38 gm/cm^3. The bulk density of powder is always less than the tapped density of its component because the powder contains inter-particle pores or voids. This statement reveals where as a powder

can only possess a single tapped density it can have many different densities, depending on the way in which the particles are packed and bed. However, a bulk density value does not necessarily simply a closed packed low porosity bed as bulk is directly proportional to tapped density.

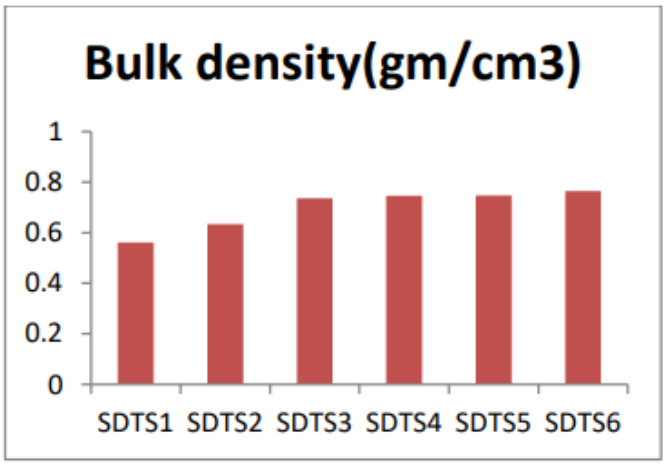

Figure 2: Pictorial presentation of Bulk density

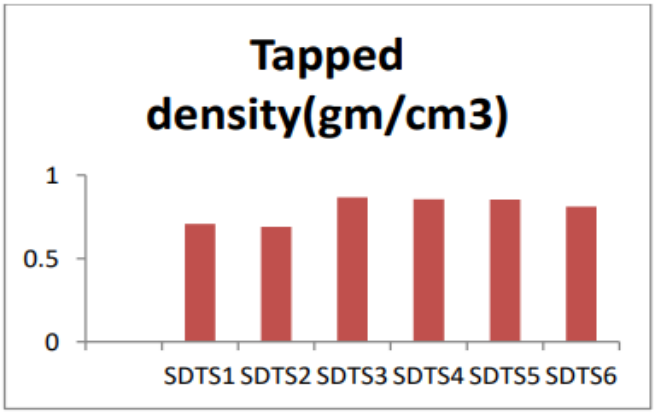

Figure 3: Pictorial presentation of Tapped density

Hausner's ratio

Hausner's ratio is another scientific and significantly good means of defining the flow properties of prepared formulation which was in the range of 1.040±0.17 to 1.26±0.43; it clearly indicate that most of the formulations having the values of Hausner's ratio are having less than 1.25, this represents that the granules have good flow property for SEDDS formulation only one formulation have the value of Hausner's ration slightly greater than the value of 1.25 it may present a little bit problem related to flow of granule may be due to rat holing.

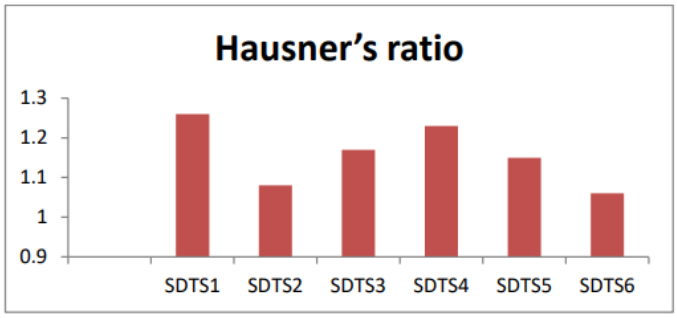

Figure 4: Pictorial presentation of Hausner's ratio Carr's compressibility index

The compressibility index of the powder is a direct measure of the potential of arch or bridge strength and stability. The determination value for Carr's compressibility index of the above formulation were found in the range of 5.5 ±0.63 to 20.76 ±0.87 % were found in the range.

which suggest that all the prepared granules having good compression property for SEDDS formulation.

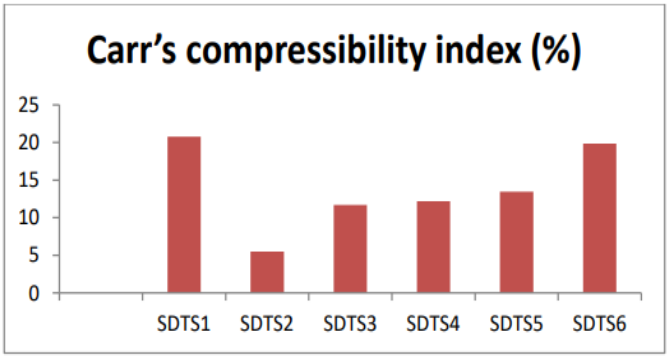

Figure 5: Pictorial presentation of compressibility index Preparation And Charecterisation of Sedds Tablets The Sedds of diclofenac sodium can be prepared by melting the surfactant mixture of tween-40 in co-solvents like PEG-6000 or span-40 by using oil like soyabean oil or Olic acid. During melting the temperature should below 70°C. The molten blend was prepared by using China dish. By using different ratio of ingredients, several formulations were prepared. Then the prepared blend is mixed with the drug until a creamy dispersion was

produced. Finally, the blended excipients (CCS, Lactose, and PVPK-30) were mixed physically in different proportions. Creamy dispersion was then mixed thoroughly until a suitable mass was obtained. Then this mass was semi-dry after semi dry it was screening and then send for full dry. After complete dry it was lubricated by using talcum (4%) and Mg. Stearate (2%) w/w then compressed as tablet.

Formulation Code	Thickness (mm) ±SD	Hardness (kg/cm²) ±SD	Friability (%)	Drug content (%)±SD	Disintegration Time (Minutes)
SDTS1	5.11±0.02	5.23±0.101	0.44±0.34	97.66±1.41	8.64 ± 0.32
SDTS2	5.14±0.002	5.78±0.23	0.45±0.15	93.36±1.46	9.55 ± 0.53
SDTS3	5.11±0.03	6.25±0.13	0.59±0.42	96.43±1.51	9.23 ± 0.48
SDTS4	5.13±0.04	5.35±0.15	0.38±0.61	95.62±0.55	8.52 ± 0.58
SDTS5	5.12±0.03	6.43±0.11	0.69±0.19	91.76±1.6	8.65 ± 0.62
SDTS6	5.15±0.07	5.67±0.12	0.54±0.3	93.33±0.56	9.75 ± 0.49

Table 2: Comparative data for evaluation of various properties of SEDDS tablets

Hardness and friability

The hardness of the tablet affects the release pattern of the drug from the formulation. Thus, SEDDS tablets must attain a sufficient strength in order to maintain the good release pattern of the formulation. Therefore, the hardness of prepared tablets was determined. The mean values of hardness of SEDDS tablets were in the range of 5.13±0.115 to 6.85±0.100 kg/cm2. The hardness of tablets increases by increasing the concentration of PVPK-30 which was attributed to binder property. All tablets showed hardness of more than 5 Kg/cm2 that reflects, the tablets were able to handling the pass the friability test. All the prepared tablet exhibited friability less than 1 % which meets the pharmacopeia standard limit, indicating that the formulation was mechanically stable.

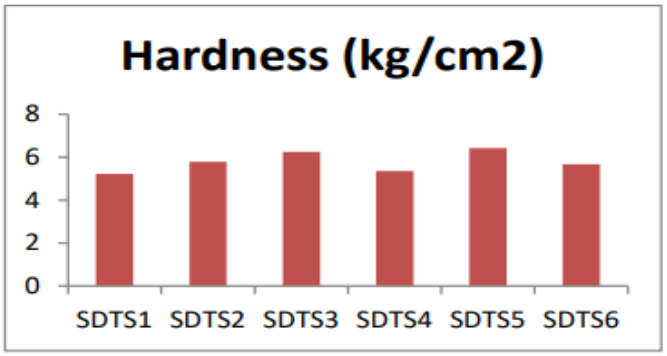

Figure 6: Pictorial presentation of hardness

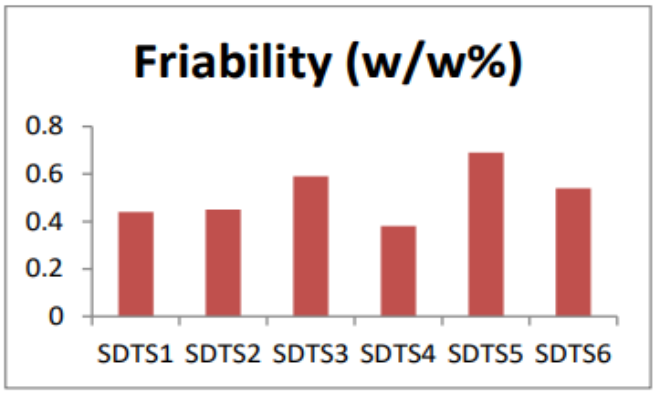

Figure 7: Pictorial presentation of Friability

Thickness

Thickness of prepared tablets was determined by using Vernier Caliper and the value of thickness ranges between 5.09±0.064 to 5.28±0.021 mm. From the testing report of tablet, it was found that the thickness exhibited by prepared SEDDS tablets did not cross the limit. this shows the efficiency of equipment and the process.

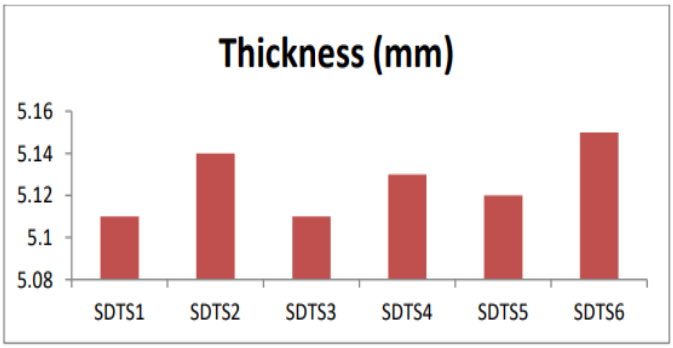

Figure 8: Pictorial presentation of thickness

Drug content determination

The prepared SEDDS tablets formulations were evaluated for their percentage drug content. The

formulation passed the drug content test as the drug content was well within the range 95.33±0.66 to 97.96±1.61, suggest that a uniformity in mixing of drug with other excipients has been carried out before compression of SEDDS tablets.

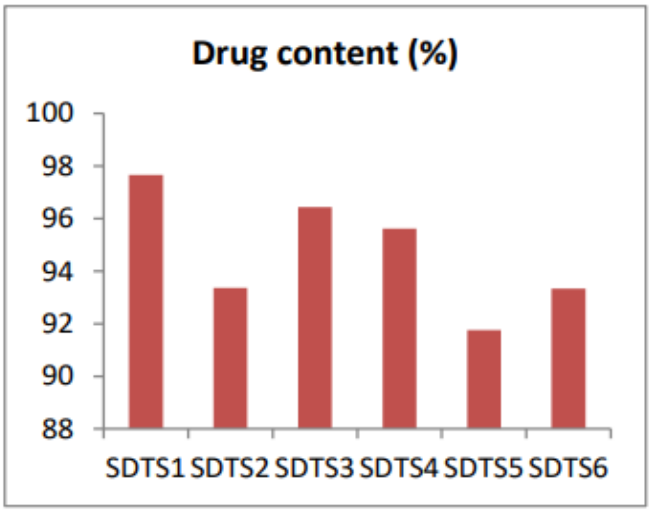

Figure No. 9: Pictorial presentation of %Drug Content

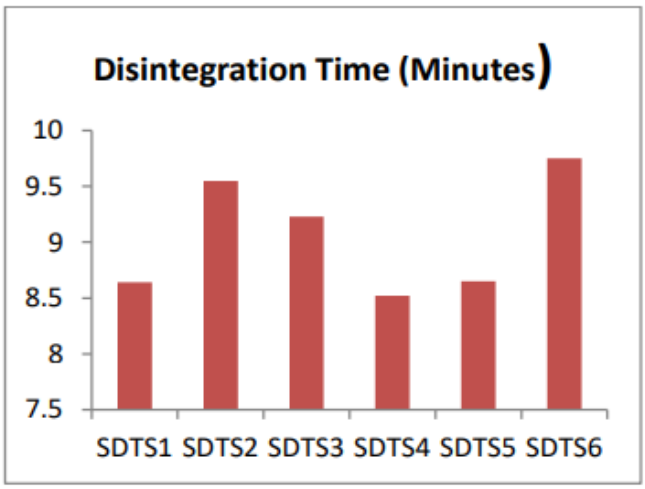

Figure 10: Pictorial presentation of Disintegration Time

In Vitro Drug Release And Release Kinetics

The release profile of formulation (SDTS1-SDTS6) along with in house developed SEDDS is displayed in figure 8.6 showed %CDR profile. The formulation SDTS1 and SDTS2 released 94.750±0.65 and 87.345±0.23 of drug within 120 min and achieve zero order kinetics. However, the formulation SDTS3, SDTS 4, SDTS 5, SDTS6 showed release of drug up to 120 minutes but Formulation, SDTS6 best modulated zero order release kinetics up to 110 minutes with maximum regression coefficient value of r2=0.9961; was optimized and compared for % CDR and release kinetics. The comparative profile of in house developed SEDDS Tablets with optimized formulation (SDTS6) showed that the in-house developed SEDDS tablet released its major part of drug within 120 minutes.

Formulation Code	Zero Order(r^2)	Higuchi(r^2)	First Order(r^2)	Peppas "n" value
SDTS1	0.978	0.981	0.976	0.58
SDTS2	0.992	0.997	0.986	0.89
SDTS3	0.970	0.987	0.964	0.62
SDTS4	0.989	0.992	0.983	0.78
SDTS5	0.984	0.989	0.976	0.59
SDTS6	0.994	0.992	0.986	0.96

*n= 3

Table 3: Mathematical modeling and drug release kinetics of SEDDS tablets

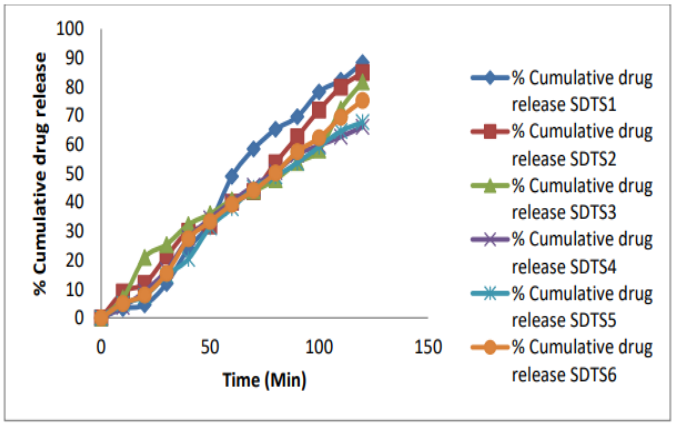

Figure 11: Zero order curve profile of prepared formulations

SEM Study: Scanning electron microscopic study of formulation treated cadaver skin clearly indicates that increased drug's penetration flux was only due to either increased hydration capacity of the applied area or by loosen the tight bounds present in-between two adjacent cells present in outermost layer of the skin (mainly responsible for presenting barrier for penetration). No sign of any type of keratolysis in applied area.

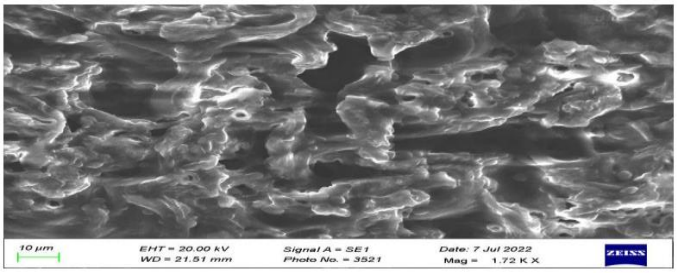

Figure 12: SEM picture of treated cadaver skin

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