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Formulation Design and Characterization of Silver Sulfadiazine Loaded Nano Gel in the Treatment of Burn

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ABSTRACT

Background: In permeation of drug, size of drug plays a very important role as size of dug as much as smaller, it become very easy to permeate so that researchers attract towards making size in nano range. Silver sulfadiazine on of the drug which is very useful in the treatment of burn. Many processes are adapted to make nanoparticles of this drug but the promising method of preparation of NPs of this drug is still vacant.

Objectives: Development of silver sulfadiazine loaded Nano gel by using Noveon polycarbophil AA-1 as gelling agent in the treatment of burn infections.

Method: First of all, nanoparticle of silver sulfadiazine was prepared by Modification Emulsification method. Then a gel was prepared by using Noveon polycarbophil AA-1 as gelling agent and varying homogenization time. Prepared formulations were subjected to evaluation accordance with standard Nano gel.

Result: The formulation of Nano gel of silver sulfadiazine was prepared successfully and evaluation data were found at satisfactory level. In order to obtain particle size in Nano range, Noveon polycarbophil AA-1 was used for modification emulsification method in which at 0.75% concentration found to bring Nano size of particle in the range 10 to 200 nm. Formulation was evaluated for % drug entrapment efficiency, cumulative % drug release, spreadability, homogeneity. pH, clarity of gel etc. All the results were found in limit and showed satisfactory level of formulation for FG-5.

Conclusion: Silver sulfadiazine loaded Nano gel by using Noveon polycarbophil AA-1 by modification emulsification method and optimum homogenization time would be very promising approach and convenient economically.

Keywords: Silver sulfadiazine, loaded, nanogel, burn, Noveon polycarbophil AA-1

INTRODUCTION

Nanoparticle formulation is taking much more interest in pharmaceuticals preparations due to its nano size make which it enables to permeate smaller pore size of cell in drug delivery systems. Nanotechnology taking a tremendous interest in present century due to its nano-size become potential in drug delivery. Nano sized hydrogel made up of highly cross linking of polymer by either co-polymerized or monomers known as Nano gel systems [1, 2]. Due to the most potential benefit of delivery of drug to the target site in sustained and controlled manner through nanomedicines became most demanding technology in the market of nanotechnology [3]. Nano gel system brings drastic revolution in the field of drug delivery by overcoming various limitation of conventional drug delivery system. In the field of polymer science, it has become inexorable to make advance nanosystems for effective treatment and for clinical trials [9].

Semisolid formulations with three-dimensional networks of organic systems comprising fluids and pharmaceuticals have been referred to as gels in the past. These technologies were primarily used in the old system of topical medication delivery for local effects [4]. With these preparations, it's possible that focused drug delivery won't be possible [8]. The importance of nano-sized microgels and hydrogels has risen as a result of the anticipated of a specialised delivery strategy. The versatility of nanogel formulations has been aided by the broad diversity of polymer systems available and the ease with which their physicochemical properties can be changed. Nanogels have been proven to have promising clinical usefulness in a recent study [5]. Nanogels have changed the field of gene therapy, as gene delivery within cellular organelles for gene silencing therapeutic systems is now achievable. Nanogels are typical formulations with a size range of 10 to 100 nm; the volume percentage can be varied by adjusting solvent quality and branching to retain a three-dimensional structure [6]. Overall, the research implies that future innovation in this field will provide solid support for cancer treatment [7]. SSD is a mixture of silver and sulfadiazine that has been widely accepted to prevent bacterial infections in second-degree burn wounds by the Food and Drug Administration (FDA) as a topical agent [10]. SSD is a polymer in which each silver ion is tetracoordinated and held by three separate deprotonated sulfa molecules, and each sulfa molecule binds three different silver ions in a sequential manner [11, 12]. In a 30 percent ammonia solution, SSD is easily soluble [12].

MATERIALS AND METHODS

Silver Sulfadiazine (SSD) drug was a gift sample obtained from Yarrow Chem product Mumbai, Noveon polycarbophil AA-1 was purchased from Chemdyes Corporation Gujrat. Other excipients such as propylene glycol, tween 80, triethanolamine, benzoic acid, methyl paraben propylparaben were obtained from Astron Chemicals Ahmedabad. Methanol of analytical grade was purchased from Fine Chemicals Ltd. Mumbai. All the chemicals were used of analytical grade.

Method of Preparation:

Preparation of SSD loaded Nanogel: For the preparation of nanogel, modified emulsification diffusion method was used in which firstly polymer was dissolved in 20 ml methanol then SSD was weighed accurately 60 mg and added to this methanol-polymer solution to get drug-polymer mixture. In other hand an aqueous solution of tween 80 for 60 ml was prepared with constant stirring at 6000 rpm using high speed homogenizer. Then drug polymer mixture was added (0.5ml/min.) into aqueous solution with the help of syringe at 6000-11000 rpm. Resulting formulation was stirred for 10 minute at high speed of 12000-24000 rpm. Then sample was sonicated 5-10 min. after that distilled water was added slowly with constant stirring for 1.5 hr. in response to get diffusion of organic solvent into continuous phase so that nanoparticle formed. Then prepared nanoparticles were incorporated into gel forming agent Noveon polycarbophil AA-1 in solution form by using stirrer. At last pH was checked and adjusted to 7.0 by Triethanolamine. SSD loaded gel was stored at room temperature [13-16].

Table 1: Silver sulfadiazine loaded Nano gel formulation table.

Ingredients (mg)	FG1	FG2	FG3	FG4	FG5
SSD	60	60	60	60	60
Noveon polycarbophil AA-1	20	40	60	80	100
Methanol	20	20	20	20	20
Tween 80	0.5 %	2 %	1.5 %	2 %	2.5%
Distilled water	20	20	20	20	20
Homogenization time	1000 rpm	2000 rpm	3000 rpm	4000 rpm	5000 rpm

EVALUATION OF NANOGEL

Particle size measurement: Size of the particles of nanogel were determined by using Zetasizer Malvern Zetasizer Ver .7.11 (6000MS). Polydispersity index were recorded by same procedure as applied for particle size determination. Zeta potential of nanogel was recorded by using same instrument Zetasizer Ver .7.11 (6000MS) (Malvern Instruments UK) as applied for both above.

Drug Content (Total): For the estimation of drug content of nanogel, firstly 1 g of prepared nanogel was taken into 10 ml methanol in volumetric flask and dissolved it then centrifuged at 5000 rpm for 16 min by using microcentrifuge (Remi). Supernatant liquid was obtained from this 1 ml of supernatant liquid was withdrawn and diluted with methanol up to 10 ml. Then diluted sample was analyzed in order to get absorbance from UV spectrophotometer (Shimadzu 1800) at 252nm wavelength. After getting absorbance, the concentration was determined by using calibration curve made previously. Calculation of total drug content (TDC) was done by using following formula [17].

$$Total\ Drug\ Content = \frac{Total\ amount\ of\ nanogel\ \times Amount\ of\ drug\ in\ 1\ g}{Weight\ of\ initial\ drug - weight\ of\ free\ drug}$$

Entrapment Efficiency: For the determination of entrapment efficiency, above procedure of drug content was applied and calculated by using following formula [18].

$$\%\ \text{Entrapment Efficiency} = \frac{Weight\ of\ initial\ Drug - free\ drug}{Weight\ of\ initial\ drug} \times 100$$

In-vitro drug release study:

In order to get drug release study, dialysis membrane diffusion method was adopted. In this method firstly a Franz's diffusion apparatus was taken and assembled. Dialysis membrane was previously soaked in phosphate buffer of pH 7.5 prepared for receptor compartment [18]. The formulation of nanogel weighed for 0.5 g and transferred into donor compartment. Dialysis membrane was cut and placed between receptor and donor compartment before transferring formulation in donor compartment [19]. Assembly was fixed and formulation of nanogel release from donor compartment to receptor compartment filled with phosphate buffer pH 7.5. An aliquot of 0.5 ml was withdrawn from receptor compartment at time interval of 0.5, 1, 2, 4, 6, 8, & 10 h respectively and immediately replaced with fresh buffer in receptor compartment. 0.5 ml withdrawal sample was further suitably diluted and analyzed by using UV spectrophotometer at 252 nm lambda max in methanol. Drug release was calculated and data was applied in various release kinetic model to see the fitting [20].

RESULT AND DISCUSSION

Physical Characterization: SSD loaded nanogel was found to be in good consistency, good homogeneity and clear transparency. It was also found to be uniform distribution and uniform dispersion. Noveon polycarbophil AA-1 at concentration of 50 mg showed optimized formulation and in better consistency.

Scanning Electron Microscopy (SEM): SSD loaded nanogel was subjected to SEM for the testing of shape and surface morphology and uniformly dispersibility. Optimized nanogel was observed by scanning electron microscopy and it was found to be particles of SSD loaded nanogel in moderately spherical shape and smooth surface. Particle size of nanogel was found to be in nanometric range as showed in figure 1. Although, some particles were found to be

clusters but mostly was in uniform dispersion and uniform distribution in respect to overall formulation [21].

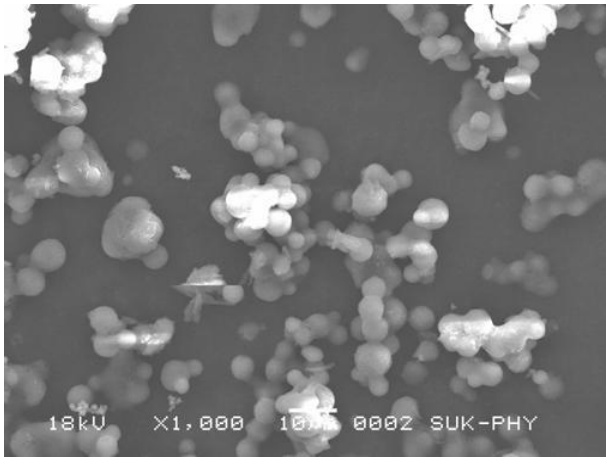

Figure 1: Particle size and suface morphology of SSD loaded nanogel of optimized formulation FG-5.

Average Particle size and Zeta potential:

Particle size of SSD loaded nanogel were subjected initially through Zeta sizer which result was revealed that the size of the particle was affected by concentration of noveon polycarbophil AA1 and homogenization time [23]. Although particle size of the formulation FG-5 was found to be within the range i.e. between 213.5 to 256.7 nm. And for the stability test, Zeta potential were used to estimate stability test of formulation in which zeta potential of formulation FG-5 was found to be between the range ± 32 mV. Zeta potential of nano formulation of SSD loaded was found to be in the range of 0.015 mV. Polydispersibility Index (PDI) of Nano formulation FG-5 was found to be in the range of 0.130 to 0.425. Distribution of drug throughout formulation. % Entrapment efficiency was found to be 82.34%.

Z-Average (d.nm): 181.8
PdI: 0.193
Intercept: 0.878
Result quality : Good

	Size (d.nm):	% Intensity:	St Dev (d.n
Peak 1:	228.7	100.0	96.59
Peak 2:	0.000	0.0	0.000
Peak 3:	0.000	0.0	0.000

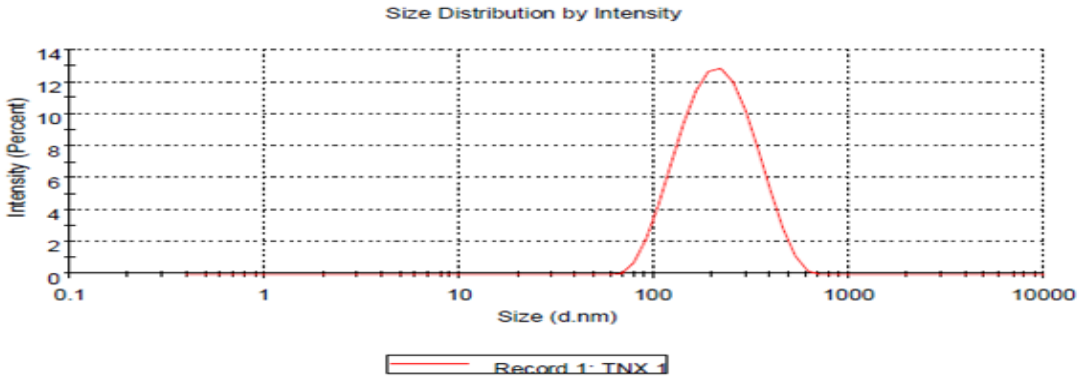

Figure 2: Particle size of SSD loaded nanogel.

Results

			Mean (mV)	Area (%)	St Dev (mV)
Zeta Potential (mV):	0.0150	Peak 1:	0.0150	100.0	4.13
Zeta Deviation (mV):	4.13	Peak 2:	0.00	0.0	0.00
Conductivity (mS/cm):	0.00449	Peak 3:	0.00	0.0	0.00
Result quality :	See result quality report				

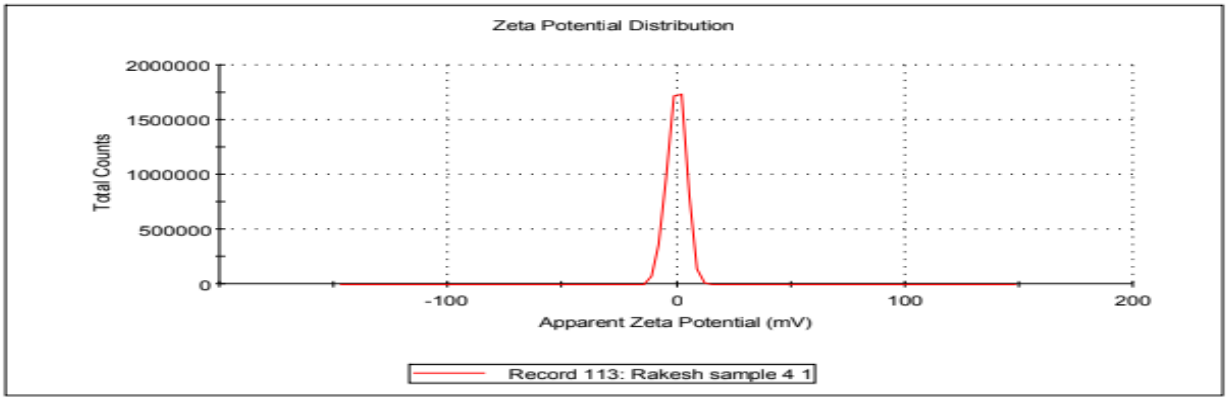

Figure 3: Zeta potential of SSD loaded nanogel.

Drug content and Entrapment Efficiency: The % drug content in the prepared formulation was found to be in different in different formulation among that optimized formulation of SSD loaded nanogel, % drug content was found to be within the limit and highest % of drug content was 91.98% in formulation FG-5. In addition, entrapment efficiency was observed and found to be satisfactory result. FG-5 formulation was found to be optimized formulation because it also showed uniform [24]

In-vitro drug diffusion studies:
From the data obtained by In-vitro drug release were observed and analyzed and revealed that drug diffusion through diffusion membrane in 24 h sustained the release only due to use of noveon polycarbophil A-A-1 polymer at concentration of 100 mg. FG-5 formulation had showed better drug diffusion among all five formulations of SSD loaded nanogel [25, 26]. Due to good homogenization time, and polymer concentration, FG-5 showed better release pattern in 24 h i.e. 92.68 %.

Table 2: In-vitro drug diffusion studies of formulation FG-1 to FG-5.

Time (h)	FG-1	FG-2	FG-3	FG-4	FG-5
0	0	0	0	0	0
1	34.31	31.23	34.14	32.46	35.95
2	41.32	38.19	38.96	46.21	43.21
3	62.12	62.38	62.98	56.31	55.92
6	72.23	67.41	64.84	67.39	68.32
9	73.24	73.15	74.26	75.23	72.62
12	79.21	82.09	87.05	80.63	84.36
24	86.48	94.05	88.16	87.82	92.68

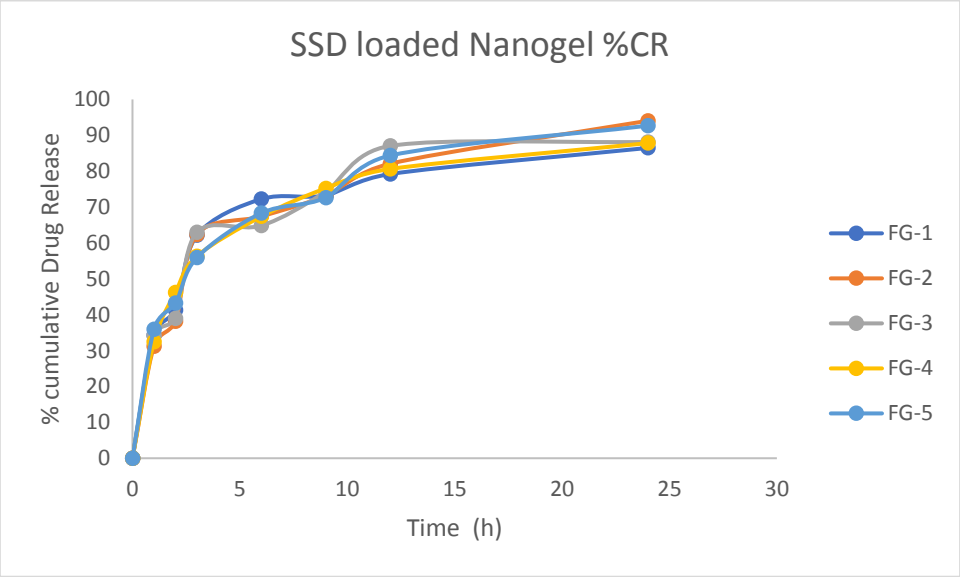

Fig. 4: Cumulative % drug release of SSD loaded nanogel formulations.

CONCLUSION

It was concluded that present investigation of SSD loaded nanogel prepared by modification emulsification method followed by homogenization can be a promising approach and result shows FG-5 was best formulation among all the formulation. So modification emulsification method, noveon polycarbophil AA-1 & 6000 RPM homogenization speed are desired and optimized selected parameters for the formulation of nanogel.

Abbreviations

SSD : Silver Sulfadiazine
RPM : Rate Per minute
TDS : Total drug Content
SEM : Scanning Electron Microscope

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Conflict of Interest: None

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