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Original Article

FABRICATION AND *IN VITRO* CHARACTERIZATION OF A NOVEL NANOSUSPENSION OF TELMISARTAN: A POORLY SOLUBLE DRUG PREPARED BY ANTISOLVENT PRECIPITATION TECHNIQUE USING 3^3 FACTORIAL DESIGN

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ABSTRACT

Objective: The motivation behind the current examination was to build the solvency and dissolution rate of an antihypertensive drug telmisartan by the planning of nanosuspension by precipitation method at the research facility scale. We researched the nanoparticle manufacture of telmisartan employing a 3^3 factorial experimental configuration considering the impacts of nanosuspension on the physical, morphological, and dissolution properties of telmisartan.

Methods: To get ready, nanosuspension particles of an ineffectively dissolvable drug are moreover of a drug solution to the anti-solvent leads to abrupt supersaturation and precipitation the making of nanoparticles. The nanosuspension particles of a poorly soluble drug loaded with urea and surfactants (sodium lauryl sulfate (SLS), poloxamer 188, Tween 80) have been prepared by a precipitation method. The nanosuspension particles were characterized for particle size, zeta potential, Fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), *in vitro* drug release, and release kinetics.

Results: The readily optimized batch nanosuspension particles evaluated and exhibited the particle size (750 nm), zeta potential (-24.33 mV), differential scanning calorimetry (DSC) drug exhibited a change in crystalline form to amorphous, *in vitro* dissolution (F12 was higher 95% within 5 min) and drug release kinetics. The formulation parameter of surfactant concentration is optimized.

Conclusion: The formulation of the nanosuspension approach has been shown to substantial improvement in the dissolution rate, thereby enhancing the oral bioavailability with the future development of this technology.

Keywords: Telmisartan, Nanosuspension, Precipitation, Dissolution, Release kinetics

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INTRODUCTION

The most convenient and universally adopted route for the drug delivery system is an oral route because it is highly flexible for designing the dosage form as contrasted with other drug delivery systems [1]. The term nanotechnology, inferred from the Greek word 'nano', meaning 'dwarf', applies to the engineering principles, natural philosophy and material science, electronics, and manufacturing at a molecular or submicron level. The nanoscale materials might be a gimmick or a system or these could be supramolecular structures, complexes, or composites. Albert Franks defined, during the former promoter of nanotechnology 'in the area of scientific discipline and technology where standard particle dimensions are from 0.1 nm to 1000 nm in range. In the mainstream biomedical applications, significant rises are made by nanotechnology, as easily as in the fields of drug release, gene therapy, imagery, and novel drug discovery systems [2, 3]. The overall rise of nanoscale science and engineering set apart by the declaration of the national nanotechnology initiative (NNI) in January 2000. Current investigation on Biosystems at the nanoscale has made one of the most unique science and technology domains at the union of physical sciences, atomic engineering, natural science, biotechnology, and drug. Nanotechnology is portrayed as a field that puts on the nanoscale benchmarks and strategies to comprehend and modify bio-systems (living or non-living) and which uses natural guidelines and constituents to make new contraptions and systems composed from the nanoscale [4]. For expanding drug markets, NDDS represents an intended tool for the pharmaceutical industries. The engineering development is assisting and enhancing pharmaceuticals such as expanding product age or can enhance their performance, either by increasing therapeutic effectiveness or improving safety and patient compliance [5]. In recent years novel drug delivery systems (NDDS) like nanosuspensions draw heavy attention in the search for improving the bioavailability of poorly soluble drugs [6, 7]. The colloidal submicron dispersal of medication particles is nanosuspension. A pharmaceutical nanosuspension characterized as finely colloid biphasic, scattered, strong medication particles in an aqueous vehicle, size underneath 1 µm, with no matrix solid, dissolved by surfactants and polymers, arranged by reasonable strategies for drug delivery applications, through different courses of administration like oral, skin, parenteral, ophthalmic and pulmonic routes. A nanosuspension does not handle poor dissolvability and bioavailability yet, furthermore, modifies the pharmacokinetics of the drug, and that enlarges drug safety and efficacy. In nanosuspension innovation, the drug kept up with the required crystalline state with decreased molecule size, prompting an expanded dissolution rate and in this way, enhanced bioavailability [8]. Nanosuspension characterized as "in a watery vehicle very fine particles are outspread, stabilized by surface-active agent, for together oral and topical use and parenteral and pulmonary administration, causing a small particle size, dissolution rate increases and thus improved bioavailability". The diameter of the suspended nanoparticles is less than 1 µm in size (i.e. 0.1 nm-1000 nm) [9-11]. Similarly, for class II drugs, which are poorly aqueous soluble and also in organic media, the problem is more complex [2]. The compounds that are polar-insoluble (oil soluble), favored for getting ready nanosuspensions with more log P-value. Consequently, the rate of the overflowing of the therapeutic action compound increases, and the maximum plasma drug level is passed quickly e. g., oral or parenteral administration of the nanosuspensions. The orally active non-peptide angiotensin II antagonist is identified as telmisartan, which takes a shot at the AT1 receptor subtype. Among commercially available angiotensin receptor blockers (ARBs), it delivers the highest affinity for the AT1 receptor and has negligible affinity for the AT2 receptor [12]. The diligence of the nanosuspension systems in the treatment of high blood pressure remains to go wider,

however; mechanization is not sufficient for many new drugs those are very less soluble, which prompted the development of nanoscale systems. By decreasing the particle size from a micrometer to a nanometer scale, in that location is a substantial increase in dissolution rate due to increasing the surface area [13, 14]. Antisolvent precipitation procedure is a promising strategy to manufacture ultrafine drug particles, which depends on the difference in super saturation brought by blending the solution and the antisolvent [15, 16]. In this current study, nanoprecipitation precipitation strategy is utilized where a drug solution in a water-miscible organic solvent blended with an aqueous solution comprising a surfactant. After blending, the supersaturated solution prompts nucleation and development of drug particles, which might be stabilized by surfactants. The fundamental target of the current investigation is to perform the preparation and evaluation of nanosuspensions of anti-hypertensive drug Telmisartan by utilizing appropriate polymers to enhance its bioavailability. A 3^3 factorial design was employed to explore the joined impact of 3 formulation variables [17].

MATERIALS AND METHODS

Materials

The gift sample telmisartan was acquired from Matrix Laboratory Limited, Hyderabad, India. Poloxamer 188 and Tween 80 was procured from Torrent Pharmaceuticals Ltd, Ahmadabad and Shreeji Pharma International, Vadodara, India. Urea and SLS bought from Rankem Pvt Ltd, India. From the authorized dealer, all other chemicals procured are analytical grade [3, 5, 18].

Methodology

Ultraviolet spectroscopy

A stock solution of telmisartan, 10 µg/ml in a buffer of 0.1 N HCL prepared and scanned in UV-Vis spectroscopy between 200-400 nm and the scanned drug λ max traced out [19-21].

Preparation of calibration curve

The 20 mg of pure drug solubilized in 20 ml of methanol and its concentration becomes 1000 µg/ml. From the above solution, 10 ml withdrawn and dissolved in 100 ml of 0.1N HCl to give concentration 100 µg/ml and is named as a stock solution. From the of prepared, 100 µg/ml stock solution, sequential dilutions set up by withdrawing 0.5, 1, 1.5, 2, 2.5 and 3 ml, which were a build-up to a volume of 10 ml each, in individual volumetric flasks to get the separate concentrations of 5, 10, 15, 20, 25 and 30 µg/ml and named appropriately. The calibration curve of telmisartan then constructed by scanning the respective serial dilutions of the drug solution (5, 10, 15, 20, 25, 30 µg/ml) using UV-Vis spectroscopy at the wavelength of maximum absorption (λ max) [19-22].

Formulation design and preparation of telmisartan nanosuspension

While formulating a steady suspension with the smallest particle size, a top nucleation rate but a low growth rate is essential. Both rates are reliant on temperature: the ideal temperature for nucleation may lie beneath that for crystal development, which grants temperature optimization. Nanosuspensions set up by the solvent evaporation procedure and by precipitation method, the nanosuspension particles of a poorly soluble drug have been prepared.

In this process, telmisartan solubilized in methanol at room temperature and it poured into an anti-solvent (water) comprising urea and separate quantity of poloxamer 188, Tween 80, SLS, or in combination in various formulations continued at room temperature and afterward stirred on a magnetic stirrer (Remi, India.). The same quantity of telmisartan and urea was mixed and rapid addition of this solution through a needle situated with the syringe, directly into stabilizer/surfactant solution holding anti-solvent leads to sudden supersaturation of the drug. Stabilizers intended to wet the outer surfaces of the particles and prevent Ostwald ripening and agglomeration to increase the stability of the preparation by providing a thick barrier on the outer surfaces of the particles and exhibit a uniform disperse stage. By evaporating organic solvents in slow magnetic stirring conditions at room temperature for 1 h the initiation of ultrafine solid crystalline or amorphous particles developed and the crystal grows in two stages one is nuclei formation and another is crystal growth [23, 24]. Afterward, prepared nanosuspension sonicated for 1 h for getting uniform size particles [25, 26].

Table 1: Formulae of telmisartan nanosuspension

Ingredients	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Telmisartan (mg)	40	40	40	40	40	40	40	40	40	40	40	40
Urea (mg)	40	40	40	40	40	40	40	40	40	40	40	40
SLS (mg)	3	5	10	-	-	-	-	-	-	-	-	-
Poloxamer 188 (mg)	-	-	-	-	-	-	3	4	5	5	5	5
Tween 80 (%)	-	-	-	0.1	0.2	0.3	-	-	-	0.1	0.2	0.3
Water (ml)	30	30	30	30	30	30	30	30	30	30	30	30

Note: (-) the particular excipient not utilized in the formulation.

Table 2: 3^3 experimental design layouts

Coded factors and units	Coded levels		
	Low level	Middle level	High level
	-1	0	1
X1: SLS (mg)	3	5	10
X2: Poloxamer 188 (mg)	3	4	5
X3: Tween 80 (%)	0.1	0.2	0.3

Experimental design

The 3^3 factorial design is one of the procedures to examine the impact of various factors on the quality determinant parameters of any formulation. Given the guideline of a plan of examinations, this structure is utilized to explore the impact of three autonomous factors. Experimental design utilized in the present inspection for the optimization of excipients concentration, such as the concentration of SLS, poloxamer 188, and Tween 80 specified as factors X_1, X_2, and X_3 learned at 3 levels each. Table 3 summarizes a record of the twelve-formulation examined, their factor combinations, and the coded levels to the experimental units utilized during the study. Formulae for all the experimental batches given in table 1 [5, 17, 27, 28].

Drug polymer interaction study

The powdered drug telmisartan and physical mixture of telmisartan and other excipients (best formulation) compatibility property originated by FTIR by utilizing Bruker Optics [29]. The compatibility study and variations in the chemical composition of the medicament after blending with excipients inspected by FTIR (Tensor 27, Bruker Optics, Germany) in the 4000-400 cm^{-1}frequency range [30].

Particle size analysis

In a microtrac blue wave-particle size analyzer, the particle size of the optimized formulation analyzed. The samples diluted with de-ionized water to get a suitable concentration for measurement [3, 18]. The particle size distribution achieved results applied to support the formation of nanosized particles [9, 23].

Zeta potential measurement

It is a term identified with the stability of samples of atoms and particles that are little enough; superior zeta potential will give stability i.e. it opposes accumulation. The zeta potential of the suspended particles of optimized formulation wares measured in Malvern zetasizer (Zetasizer 3000 HS, Malvern instrument, UK). A laser is available in the zetasizer, which employed to give light energy to illuminate the particles within the sample. When the splitting of light makes an incident and a reference beam, the zeta potential is assessed. Through the middle of the sample cell when the incident laser beam reaches, the scattered light at a 130 ° angle is detected. Zetasizer nano software generates a frequency spectrum from which the electrophoretic mobility thus, the zeta potential forecasted [21, 28, 31, 32].

Differential scanning calorimetry

Pure drug and drug-loaded optimized formulation nanosuspensions containing drug telmisartan DSC analysis carried out using DSC Q20 (TA Instruments, USA) to examine any potential drug-polymer interaction. The sample drug and nanosuspension weighed 5 mg and 5.2 mg under a nitrogen flow of 25 ml min^{-1} heated at a scanning rate of 10 °C min^{-1} the analysis performed from temperature range 25 °C to 300 °C. Utilizing TA instruments (version: 4.5A) universal analysis 2000 software, thermal data analysis of DSC thermograms directed [33-35].

Scanning electron microscopy

The surface morphology specimen originated with the assistance of a SEM, Model JSM 84 0A, JEOI, Japan. In a vacuum desiccator, the samples are becoming completely dry by using double-sided adhesive tape, before climbing up on brass specimen studies. The gold-palladium alloy of 12 nm knee coated on the sample sputter coating unit (Model E5100 Polaron U. K) using argon at an ambient of 8-10 plus plasma voltage around 20 mA. The sputtering was accomplished for about 5 min to get uniform covering on the sample to empower outstanding quality SEM pictures. The SEM was functioning at a less accelerating voltage of around 20 kV with a burden current around 80 mA [27, 36].

Dissolution study

The *in vitro* drug release studies performed in USP dissolution apparatus Type II (paddle type) (Labindia DS-800) at 50 rpm. The dissolution test operated out in 0.1 N HCl 900 ml dissolution medium and temperature at 37.0±0.5 °C. 5 ml of the test sample pulled back from the dissolution basket periodically and replaced with an equivalent volume of fresh 0.1 N HCl after every sampling. The 5 ml 0.1 N HCl withdrawn samples suitably diluted and passed through a filter paper (0.22 µm, Whatman Inc., USA) [17, 18]. The filtrate was then subject to the UV-Vis spectrophotometric analysis against the blank (0.1 N HCl). With the help of the UV-Vis spectrophotometric standard calibration curve data, the percentage cumulative drug release estimated out at 291 nm (T60 UV-Visible Spectrophotometer, Labindia Analytical) [37, 38].

***In vitro* drug release kinetic study**

The drug kinetics release mechanism achieved from hydrophilic matrices and the dissolution outcome of the respectively nanosuspension batch was processed with various kinetic equations, known as zero and first-order kinetics, Higuchi, Hixson-Crowell and Korsmeyer-Peppas model. To find out the kinetics release, information got from *in vitro* drug release readings plotted in different models of kinetic.

Zero-order model

From, the pharmaceutical dosage forms dissolution of the drug does not disaggregate and release the drug slowly (expecting that the particle surface area does not alter and no equilibrium situations acquired) and the graph plotted as % drug released Vs time in an 'h' can be expressed by

$$Q_t = Q_0 + k_0 t \quad \text{.... (1)}$$

Where, Q_0 = initial concentration of drug at time t = 0, Q_t = amount of drug dissolved at a time t, K_0 = zero-order constant in concentration/time, t = time in an 'h' [39, 40].

First-order model

The utilization of this model to drug dissolution characteristics was first intended by Gibaldi and Feldman (1967) and thereafter by Wagner (1969). This model is the necessity to decide the absorption and/or elimination of some drugs, regardless of whether it is hard to conceptualize this mechanism on a hypothetical premise. The diagram was a conspiracy as a log % cumulative drug last Vs time in an 'h' [39, 40].

$$Log\ Q_t = log\ Q_0 - Kt\ /2.303 \quad \text{.... (2)}$$

Where Q_t = percent of drug remaining at time t, Q_0 = initial concentration of the drug, K = first-order constant, t = time in an 'h'.

Higuchi model

It is a first mathematical model that defines drug release from a matrix system, recommended by Higuchi in 1961. This model depends on a various hypothesis that (1) Primary drug concentration in the matrix is lot elevated than drug solubility, (2) Drug diffusion happens just in one dimension (Edge impact should be shunned), (3) Drug particles are far lesser than the thickness of system, (4) expanding of matrix and dissolution are minor or negligible, (5) Drug diffusivity is steady, (6) Accurate sink condition constantly achieved in the release environment. The intrigue graph drowned % cumulative drug discharged Vs square root of time [39, 40].

$$Q_t = K_H t^{1/2} \quad \text{..... (3)}$$

Where, Q_t = amount of drug released at a time 't' per unit area A, K_H = Higuchi dissolution constant reflecting design variable system, t = time in an 'h'.

Hixon crowell model

The particles that have a uniformed size, the equation derived by Hixson and Crowell describes the dissolution rate based on the weight of the particles cube root and the particle radius not assumed to be variable. It is calculated by the equation,

$$Q_0^{1/3} - Q_t^{1/3} = K_H t \quad \text{.... (4)}$$

In the pharmaceutical dosage form, the incipient amount of medicament is Q_0 and the rest of the measure of medication in the pharmaceutical dosage form is Q_t at a time 't' and 'K_H' is a Hixson-Crowell proportionality consistent. From the acquit kinetics, information acquired from *in vitro* medicament release studies plotted as the cube root of % medicament remaining Vs time in an 'h' [39, 40].

Korsmeyer Peppa's model

$$M_t/M_\infty = K\ t^n \quad \text{.... (5)}$$

Where the quantity of drug release at the time 't' is Mt, and the amount released at a time is M∞ *where* t =∞, thus Mt/M∞ is at a time 't' fraction of drug released, the kinetic constant is known as 'k', and diffusion exponent is 'n' and for both solvent penetration and drug release mechanism characterized by the above equation. The correlation coefficient set up by executing the obtained data into various kinetic models and the greatest fit model affirmed by the estimation of the correlation coefficient close to 1 [19]. From the slope, the rate constants of respective models are calculated. The information was introduced for the most suitable model. If 'n' for (sphere) worth is 0.43 or a smaller amount, the mechanism of release pursues "fickian diffusion," and upper estimations of 0.43-

0.85 for the transport of mass pursue a non-fickian (anomalous transport) model. If the 'n' worth is 0.85 that means case II transport and the drug release pursues the Higuchi model. For the estimations of 'n' upper than 0.85, the mechanism of drug release is viewed as super case II transport [41, 42].

RESULTS

λ max and calibration curve

Calibration curves of telmisartan in a buffer of 0.1 N HCL solutions built at λ max recorded 291 nm with a (T60 UV-Visible Spectrophotometer, Labindia Analytical). Beer's law followed to construct the calibration curve was in the concentration range of 5-30 µg/ml. The standard graph of telmisartan demonstrated great linearity with an R^2 of 0.998, which indicates that it complies "Beer-Lambert's" law (fig. 1). The examination was done in triplicate [19, 21, 23].

Experimental data analysis

The 3 factors, 3 levels of the factorial design implemented for improvement. The SLS, poloxamer 188 amount and Tween 80 varied as stated in the strategy in table 3. Throughout the experiments entire the other processing variables, urea and water maintained fixed. Trial preliminaries were conducted at all 12 potential combinations [5, 17].

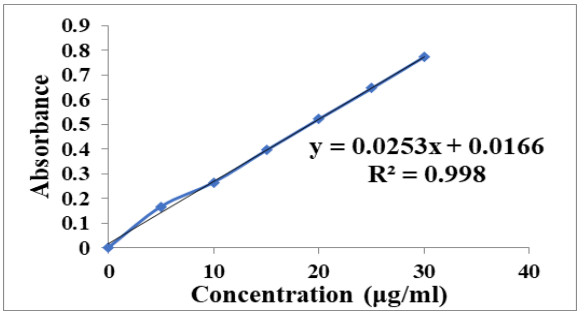

Fig. 1: Calibration curve of drug telmisartan mean of triplicate data specified (n= 3±SD)

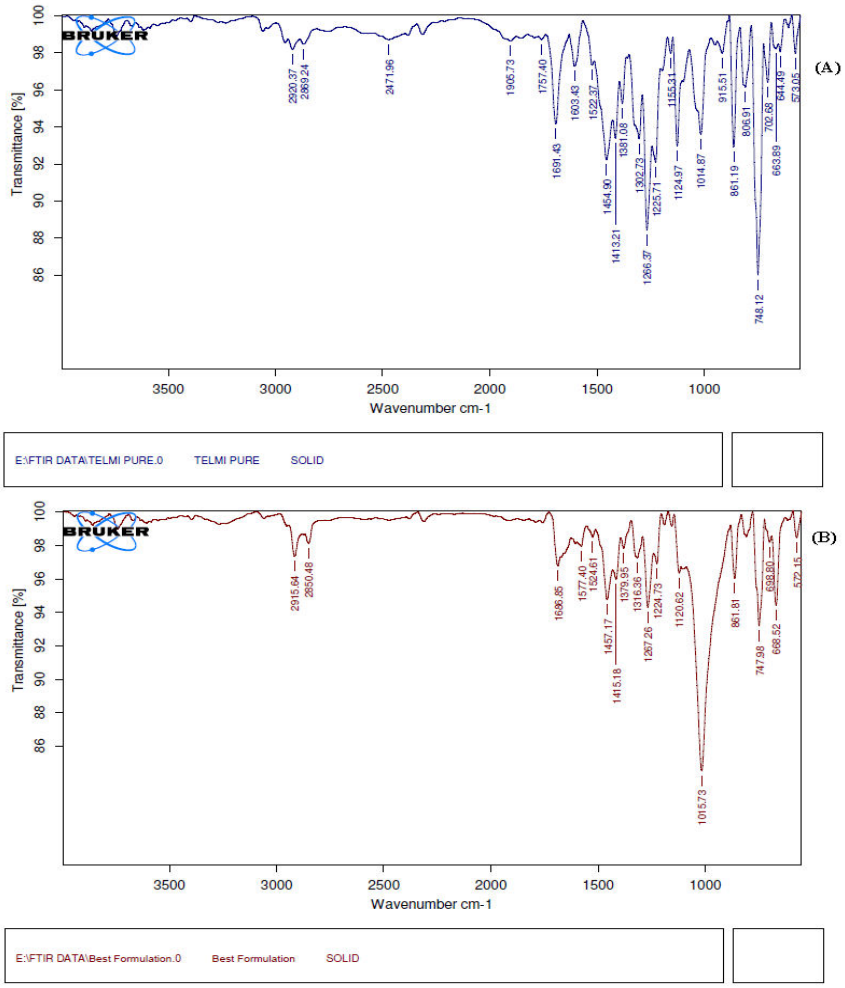

Fig. 2: FTIR spectrum of telmisartan (A) optimized formulation (B) scanned from 4000 cm^{-1} to 400 cm^{-1}

DISCUSSION

Drug polymer interaction study

The FTIR spectra of telmisartan nanosuspensions are shown in (fig. 2). Drug spectrum showed prominent peaks at 1691.43 cm, 2869.24 cm, 1603.43 cm, 1381.08 cm, and 1757.40 cm correspondings to C=N-CH_3 imine stretching, C-H alkane, C=C aromatic stretching, C-N 3° amine stretching, and C-N stretching, respectively. Telmisartan nanosuspension shows similar peaks 1686.85 cm, 2850.48 cm, 1577.40 cm, 1316.40 cm that corresponding to the C=N-CH3 Imine, C-H Alkane, C=C Aromatic, C-N 3° amine of the FTIR spectra of pure drug, which shows no interaction amongst drug and polymer [28, 30, 36].

Table 3: Formulation characteristics of 3^3 factorial design

Formulation code	Coded factors and their levels			Coded factors and their actual values		
	X1	X2	X3	X1	X2	X3
F1	-1	-	-	3	-	-
F2	0	-	-	5	-	-
F3	1	-	-	10	-	-
F4	-	-	-1	-	-	0.1
F5	-	-	0	-	-	0.2
F6	-	-	1	-	-	0.3
F7	-	-1	-	-	3	-
F8	-	0	-	-	4	-
F9	-	1	-	-	5	-
F10	-	1	-1	-	5	0.1
F11	-	1	0	-	5	0.2
F12	-	1	1	-	5	0.3

Note: (-) the particular excipient not utilized in the formulation

Zeta potential measurement

The average particle size of the drug in the optimized nanosuspension formulation (F12) was found to be approximately 750 nm. The surface potency properties and along with the extended physical stability of the nanosuspensions, were carried out by zeta potential (fig. 3). The zeta potential of the formulation was found to be-24.33 mV, so it is sufficient for maintaining stable nanosuspension formulation in the presence of poloxamer 188 and Tween 80 [27, 28, 33].

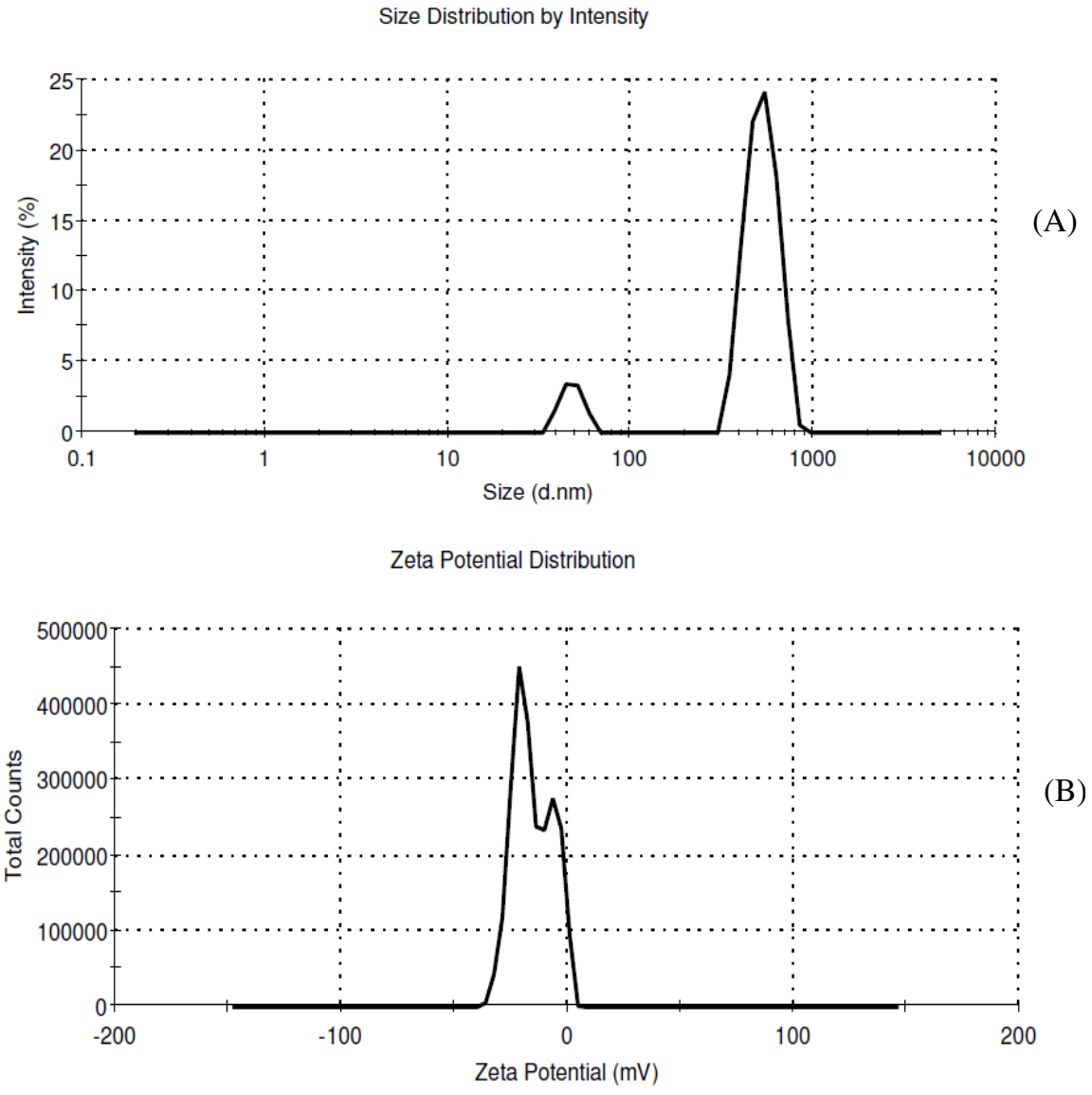

Fig. 3: Size distribution and zeta potential of optimized nanosuspension (A) and (B)

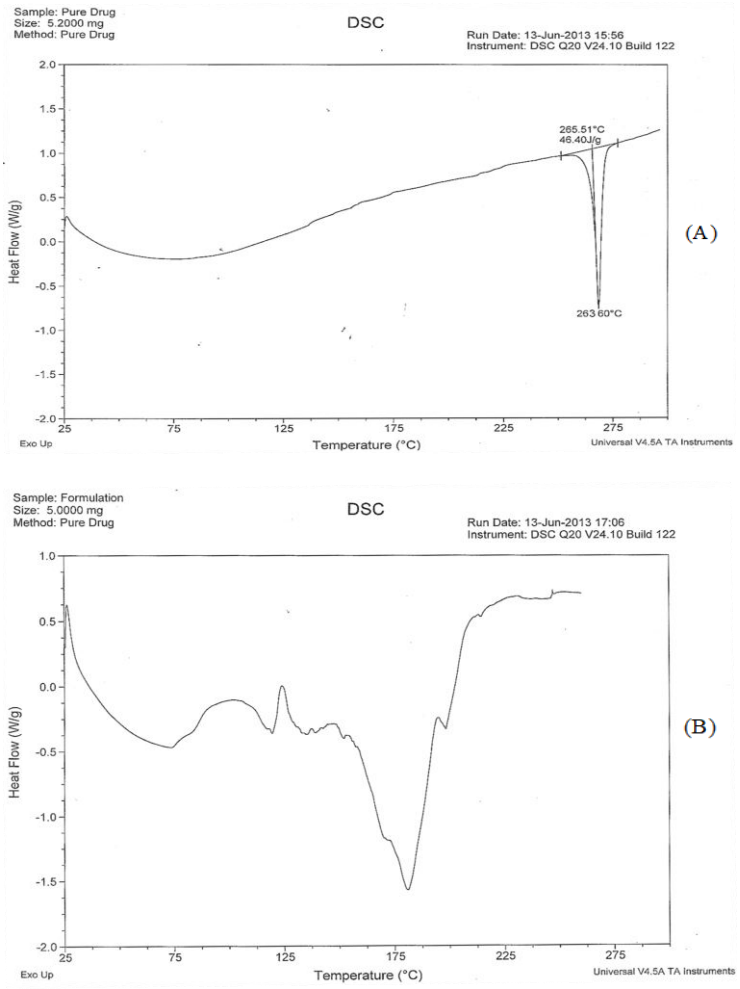

Fig. 4: DSC graph of the pure drug (A) and optimized formulation (B) scanning rate of 10 °C min^{-1} and the analysis temperature range 25 °C to 300 °C

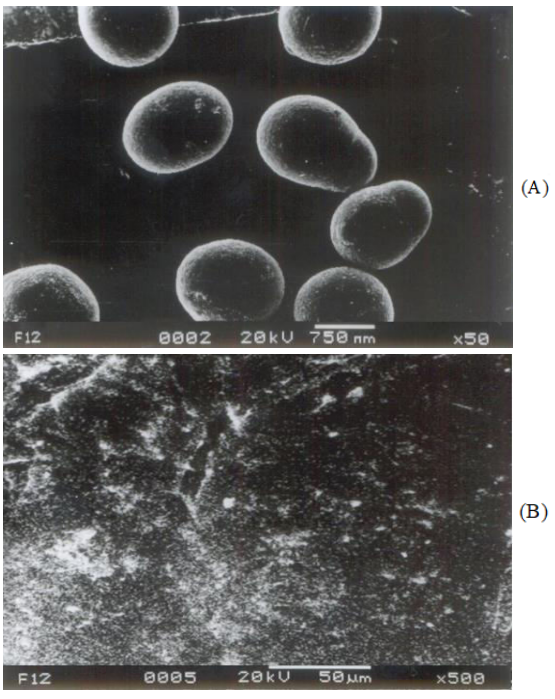

Fig. 5: SEM photographs of nanosuspension at 50x magnification (A) and 500x magnification (B)

Differential scanning calorimetry

DSC diagram demonstrates that the pure drug temperature (263.3 °C) reduced compared to the optimized nanosuspension formulation (F12) temperature (180 °C) is due to the drug charges from a crystalline state to an amorphous state. Generally, amorphous substances having a lower melting temperature than the crystalline substances in the manufacture of nanosuspension by precipitation technique. So crystalline substances having diminished solubility than the amorphous substances. The melting point of telmisartan found to be 261-263 °C, which complied with British Pharmacopoeia standards, thus indicating the purity of the obtained drug sample (fig. 4) [30-32].

Scanning electron microscopy

Surface morphology and shape of optimized formulation nanoparticles imagined utilizing SEM (Model JSM 84 0A, JEOI, Japan). The drug-entrapped nanoparticles were looking like a smooth surface (fig. 5). The drug-loaded nanoparticles were observed to be, black color with a smooth surface and almost spherical. All nanoparticles' shapes and sizes are having almost uniform. In an SEM study, the nanoparticles' surface morphology and patterns visualized [20, 31, 38].

Dissolution study

The telmisartan nanosuspension contains all the 12 formulations subjected to dissolution studies (fig. 6). In USP apparatus Type II, the dissolution test carried out by taking a 900 ml volume of dissolution media containing 0.1 N HCl solutions with a rotation speed of peddle at 50 rpm. The formulation F1 drug release rate was slower than the F2 and F2 drug release rate, also slower than F3, as a consequence of the increased concentration of SLS. The drug release rates between F4, F5, and F6 has observed that F6 (85% within 5 min) release rate was faster than the F5 (56% within 5 min) and F4 (44% within 5 min) was due to increasing the concentration of Tween 80 in the increased order from F4 to F6. By adding poloxamer 188 concentrations, in increased order i.e. 3 mg, 4 mg, and 5 mg from F7 to F9, it noticed that the drug release rate is in ascending order from F7 (73% within 5 min), F8 (80% within 5 min) to F9 (89% within 5 min). By monitoring the drug release rate data from F10 to F12 it concluded that the release rate of F12 was higher (95% within 5 min) than the F11 (90% within 5 min) and F11 release rate is higher than F10 (89% within 5 min) due to the employment of two stabilizers in which ace is in a fixed amount i.e. 5 mg and another are in increasing order (0.1%, 0.2%, 0.3%) (table 1, fig. 6). The release rate between three polymers observed that poloxamer 188 having more release rate than the other two polymers (SLS and Tween 80). F12 is the optimized formulation because the drug releases for the F12 formulation is 95.45% in 5 min. This formulation contains stabilizers, particularly poloxamer 188 and Tween 80 [37, 38, 43].

***In vitro* drug release kinetic study**

To decide the release model which best portrays the model of drug release, the *in vitro* release information is substituted in different models, for example, zero and first order, Higuchi, Hixon Crowell, and Korsmeyer Peppas kinetics models. From the release kinetics information (table 4) it affirmed that the formulations F3 and F9 obeyed the Higuchi kinetic model, which confirms that quick release of hydrophobic drug and F4, F5, and F7 obeyed Hixon-Crowell release. F8 follows zero-order release and F1, F2 and F6 follow the first-order release mechanism. The data indicate that the nanosuspension formulations F2 to F5 the drug release followed by the Fickian transport mechanism ($n<0.43$), whereas formulation F1, released the drug followed by non-Fickian (anomalous) transport mechanism ($0.43<n<0.85$) [42, 44].

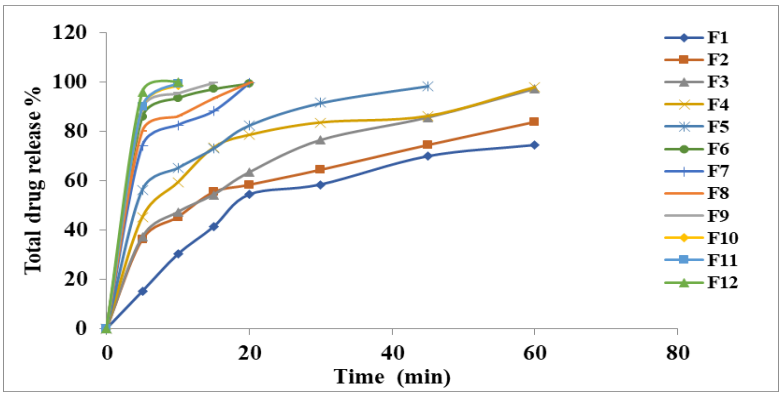

Fig. 6: *In vitro* drug release profile of telmisartan nanosuspension mean of triplicate data specified (n= 3±SD)

Table 4: *In vitro* drug release kinetic studies

Formulations	Zero-order	First-order	Higuchi	Hixon crowell	Release exponent
	R^2				(n)
F1	0.847	0.942	0.938	0.915	0.786
F2	0.760	0.987	0.986	0.982	0.333
F3	0.956	0.942	0.994	0.986	0.376
F4	0.805	0.898	0.900	0.921	0.398
F5	0.997	0.979	0.979	0.998	0.266
F6	0.924	0.999	0.968	0.998	-
F7	0.940	0.974	0.984	0.995	-
F8	0.999	0.970	0.987	0.916	-
F9	0.989	0.923	0.999	0.975	-
F10	1	1	1	1	-
F11	1	1	1	1	-
F12	1	1	1	1	-

Note: (-) the particular result doesn't originate in the formulation, (R^2 = regression coefficient, n = release exponent)

CONCLUSION

A nanoprecipitation method produced to prepare nanosuspension of telmisartan using urea as a carrier and different concentrations of poloxamer 188, Tween 80, and SLS as a wetting agent. In the nanoprecipitation method, the particle size of telmisartan can be accomplished in the nanometer in size, by modifying operation parameters, like stabilizer concentration (% w/v). The best nanosuspension of telmisartan can be obtained by urea, poloxamer 188, and Tween 80 using nanoprecipitation methods. A dissolution study in 0.1 N HCl solution shows that nanosuspension formulations F10, F11, and F12 drug releases within 10 min. Nanosuspensions represent a promising option to current drug delivery systems aiming to improve the biopharmaceutical performance of antihypertensive drug telmisartan with poor water solubility. Nanoprecipitation could thus be able to be a straightforward and effective way to deal with produce submicron particles of meanly weaken water-soluble drugs for upgrading solubility and bioavailability.

STATEMENT OF HUMAN AND ANIMAL RIGHTS

This clause does not contain any studies with human or animal subjects performed by any of the writers.

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AUTHORS CONTRIBUTIONS

From all 6 authors Sireeshaparticipated in the experimental work and Prasanta Kumar Mohapatrasupervised the entire project and writing of the manuscript. Bibhuti Prasad Rath, Harish Chandra Verma, Vaibhav Rathore, and Satyajit Sahoo have discussed the results and helped to write the manuscript. Prasanta Kumar Mohapatra acted as the corresponding author.

CONFLICT OF INTERESTS

The authors have declared no conflict of interest.

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