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Research

A study on invitro Charectarisation of Paliperidone Nanosuspensions

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Abstract

Paliperidone is a SR (5-HT2) receptor antagonist and D2DR inhibitor was BCS class II drug with low water solubility and the absolute oral bioavailability of Paliperidone following Paliperidone administration is 28%. So, it is essential to improve the solubility to enhance its bioavailability. Nanosuspension technique is a modern and a more innovative approach used widely to increase the solubility of the drug moieties. Nanosuspension of Paliperidone by solvent evaporation method using various polymers such as SLS, Pluronic F127, PVP-K90, PVA, and methanol. IR spectroscopic studies indicated that there are no drug-excepient interactions. All the prepared formulations were found to be having drug content within acceptable limits in the range of 79.26 to 97.52 % and Entrapment efficiency was found to be in the range of 82.16%-96.20% respectively. From the in vitro dissolution studies by comparing to other all the formulations F9 is the best formulation which showed 99.86% of drug released respectively within 60 min and follows Zero order release kinetics.

Keywords: Paliperidone, pluronic F127, PVP-K90, PVA, Scanning Electron Microscopy(SEM), UV Spectroscopy.

INTRODUCTION

Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biological parameters pertinent to their performance. Despite tremendous advantages in drug delivery, the oral route remains the most preferred route for the administration of therapeutic agents because of the low cost of therapy and ease of administration leads to high-

level of patient compliance. On the other hand, this high-throughput screening process has done little to address the issue of poor bioavailability of orally administered drug candidates.

During the past two decades, numerous oral delivery systems have been developed to act as drug reservoirs from which the active substance can be released over a defined period of time at a predetermined and controlled rate.

Oral drug delivery system (oral DDS) has been known for decades as the most widely utilized route for drug administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. More than 50% of drug delivery systems available in the market are oral DDS.

Pre-formulation studies

Prior to the development of dosage form, it is essential that certain fundamental physical and chemical properties of the drug molecule alone and when combined with excipients are determined. This first learning phase is known as pre-formulation. The overall objective of the pre-formulation is to generate information useful to the formulator in developing stable and bioavailable dosage forms which can be mass produced. The goals of pre-formulation studies are:

- To evaluate the drug substance analytically and determine its necessary characteristics
- To establish its compatibility with different excipients.

RESULTS AND DISCUSSION

Determination of melting point

The melting point of Paliperidone was found to be in range of 110° C which was determined by capillary method.

Saturation Solubility

Saturation solubility was carried out at 25°C using 0.1N HCL, 6.8 phosphate buffer, and purified water.

Table 1: Solubility data

Solvent	Solubility(mg/ml)
Acetone	0.852
Ethanol	0.792
Methanol	0.916
Purified water	0.014
0.1N HCL	0.129
4.5pH acetate buffer	0.152
pH 6.8 phosphate buffer	0.210
pH 7.4 phosphate buffer	0.186

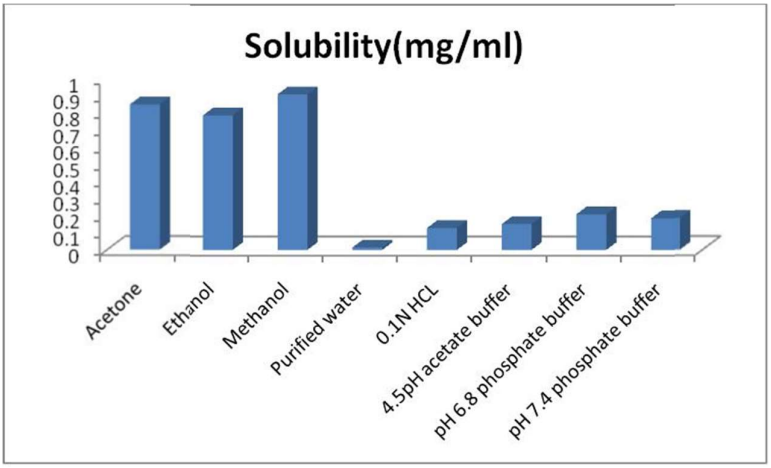


Fig 1: Solubility studies of Paliperidone

From the above conducted solubility studies in various buffers we can say that pH 6.8 phosphate buffer has more solubility when compared to other buffer solutions. So Ph 6.8 buffer is used as dissolution medium, based upon the solubility studies on organic solvents methanol has more solubility than others so methanol was used in the nanosuspension formulation.

Determination of absorption maximum (λmax)

Determination of Paliperidone λ-max was done in pH 6.8 buffer medium for accurate quantitative assessment of drug dissolution rate.

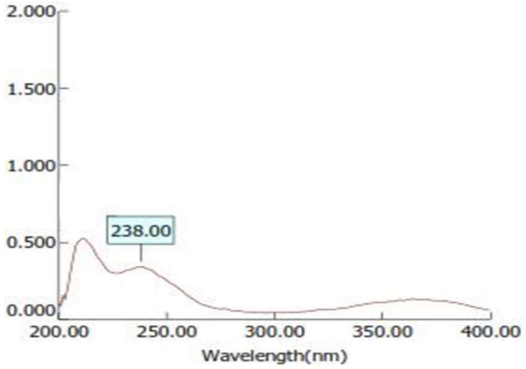


Fig 2: Uv Spectrum Of Paliperidone

Table 2: Standard graph of Paliperidone in pH 6.8 (λmax 238 nm)

Concentration (µg/ml)	Absorbance
0	0
5	0.125
10	0.257
15	0.401
20	0.556
25	0.678
30	0.824

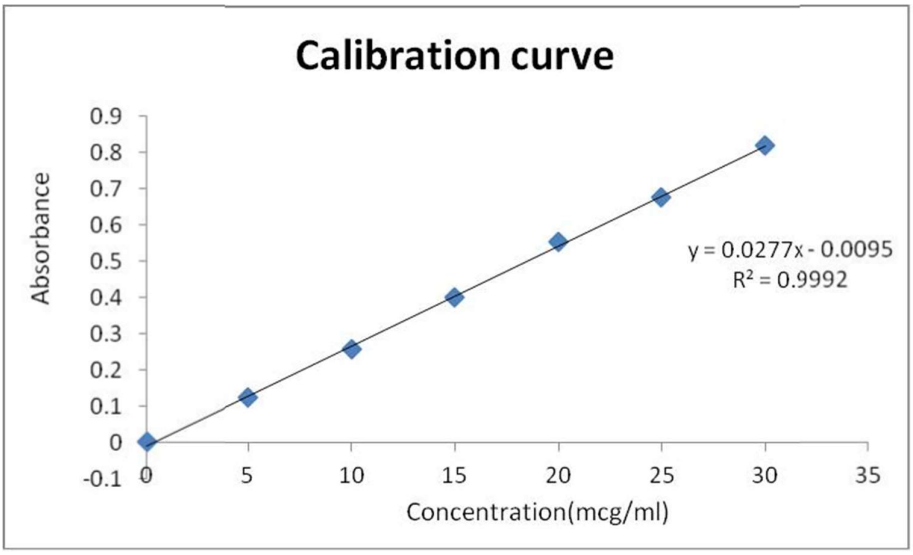


Fig 3: **Standard calibration curve of Paliperidone in pH 6.8**

The linearity was found to be in the range of 5-30 µg/ml in acetone, pH 6.8 buffer. The regression value was closer to 1 indicating the method obeyed Beer-lamberts' law.

Drug excipient compatibility

Drug and excipient compatibility was confirmed by comparing spectra of FT-IR analysis of pure drug with that of various excipients used in the formulation.

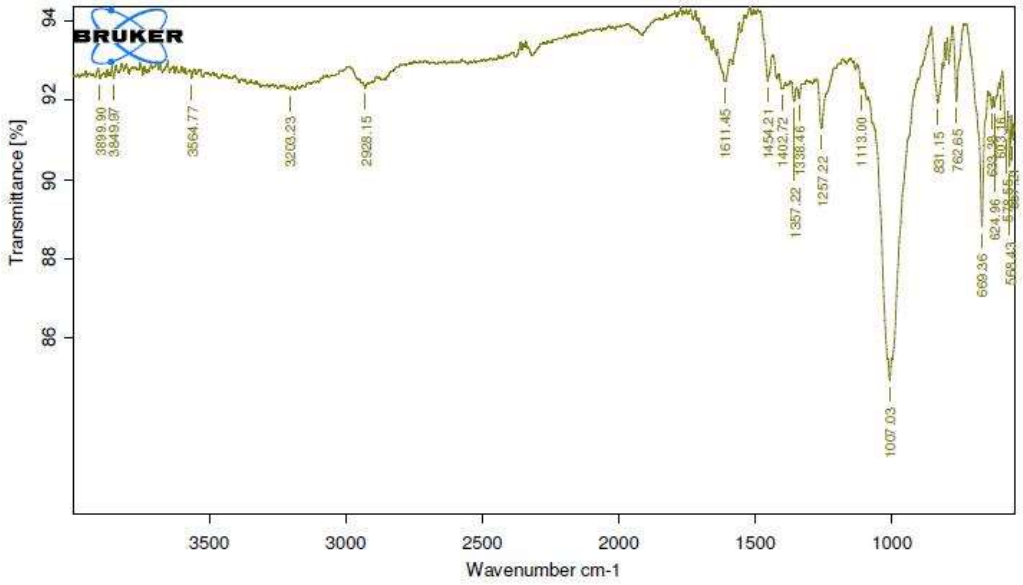


Fig 4: IR spectrum of Paliperidone

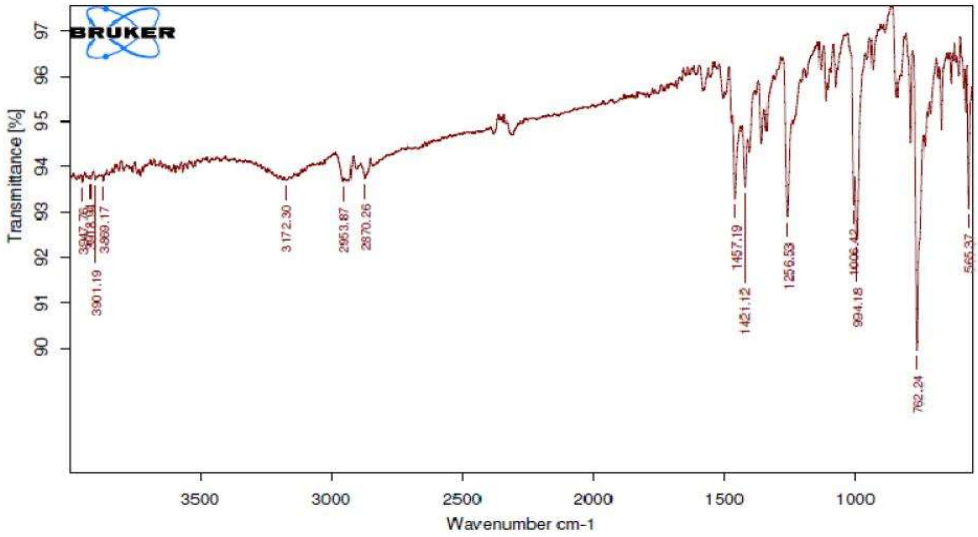


Fig 5: IR spectrum of Paliperidone Optimised Formulation

Form the drug excipient compatibility studies we observe that there are no interactions between the pure drug (Paliperidone) and optimized formulation (Paliperidone+ excipients) which indicates there are no physical changes.

Drug content

The drug content of the formulated Nanosuspension was found in the range of 78.23 to 96.45 % respectively.

Table 3: Drug content of Formulated Nanosuspension

Formulation code	Mean % drug content
F1	79.26
F2	81.02
F3	82.24
F4	84.22
F5	89.64
F6	92.31
F7	88.42
F8	92.76
F9	97.52

The percentage of drug content of formulation F1 was found to be 79.26%formulation F2 was found to be 81.02%formulation F3 was found to be 82.24%, formulation F4 was found to be 84.22%, formulation F5 was found to be 82.64%, formulation F6 was found to be 92.31%, formulation F7 was found to be 88.42%, formulation F8 was found to be 92.76%, formulation F9 was found to be 97.52%.

Entrapment efficacy

The entrapment efficacy of the formulated Nanosuspension was found to be in the range of 82.16%-96.20% respectively.

Table 4: Entrapment efficiency of formulated Nanosuspensions

Formulation code	Mean % entrapment efficiency
F1	82.16
F2	86.14
F3	88.48
F4	91.36
F5	89.62
F6	90.48
F7	92.38
F8	94.92
F9	96.20

The entrapment efficacy of formulation F1 was found to be 82.16%, formulation F2 was found to be 86.14%, formulation F3 was found to be 88.48%, formulation F4 was found to be 91.36%, formulation F5 was found to be 89.62%, formulation F6 was found to be 90.48%, formulation F7 was found to be 92.38%, formulation F8 was found to be 94.92%, formulation F9 was found to be 96.20%.

Scanning electron microscopy

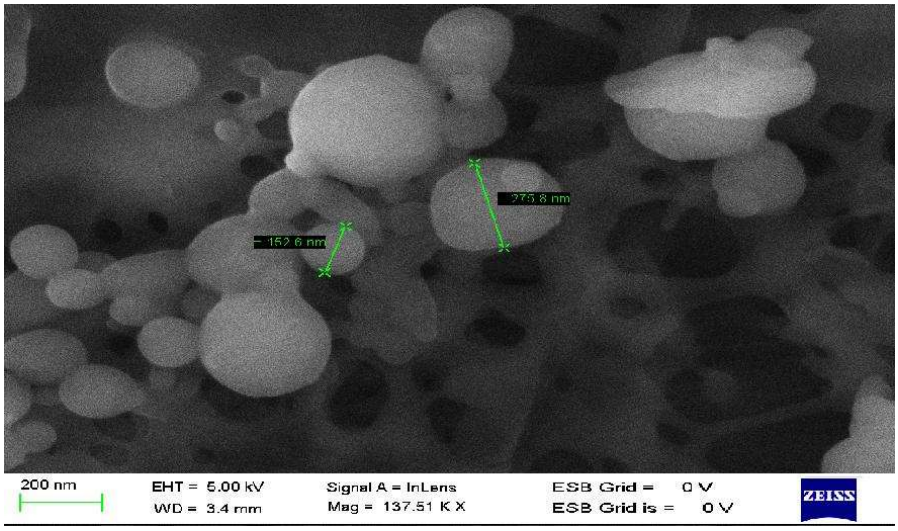
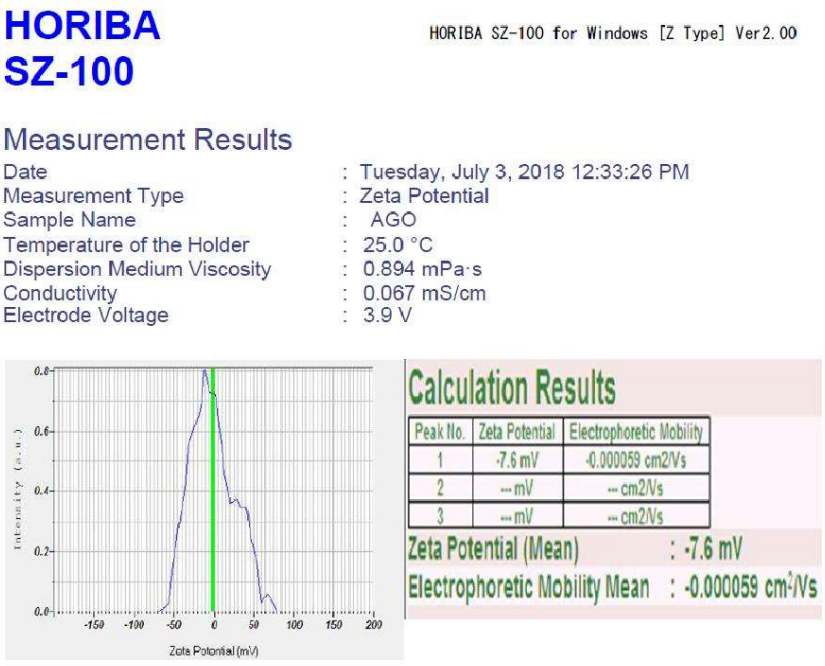


Fig 6: Scanning Electron Microscopy Of Optimized Formulation

Zeta Potential

The measurement itself is a particle electrophoresis, the particle velocity is determined via the doppler shift of the laser light scattered by the moving particles. The field strength applied was 20 V/cm. The electrophoretic mobility was converted to the zeta potential in mV using the Helmholtz-Smoluchowski equation. At standard measuring conditions (room temperature of 25°C, water) this equation can be simplified to the multiplication of the measured electrophoretic mobility (µm/cm per V/cm) by a factor of 12.8, yielding the ZP in mV.



Zeta potential value for the optimized formulation(F9) was found to be within the acceptable limits.

Particle size analysis

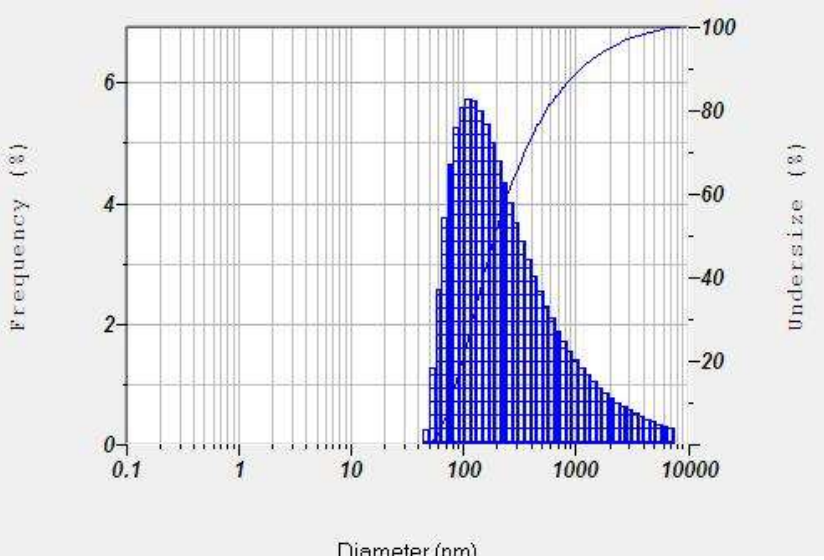


Fig 7: Particle Size Analysis Of Optimized Formulation

Average particle size of nanosuspension of optimized formulations (F9) was found to be having maximum particles at a range of 118 nm.

Paliperidone is the primary active metabolite of the older antipsychotic Risperidone. While its specific mechanism of action is unknown, it is believed that Paliperidone and Risperidone act via similar if not the same pathways. Paliperidone is also active as an antagonist at alpha 1 and alpha 2 adrenergic receptors and H1 histaminergic receptors, which may explain some of the other effects of the drug. It is a white to yellow non-hygroscopic powder and poorly soluble in water. The absolute oral bioavailability of Paliperidone following Paliperidone administration is 28%. So, it is essential to improve the solubility to enhance its bioavailability. In present investigation Nanosuspensions of paliperidone was prepared by solvent evaporation method. The Nano suspensions are novel promising target and controlled released dosage form which is gaining importance because of ease of manufacturing and diversified applications. The present trend of pharmaceutical research lies in the usage of biodegradable polymer because of its availability and low toxicity.

CONCLUSION

From the present study, oral Nanosuspension of Paliperidone by Solvent evaporation method using various polymers such as SLS, Pluronic F127, PVP-K90, PVA, and methanol. All the prepared formulations were found to be having drug content within acceptable limits in the range of 79.26 to 97.52 % respectively. All the prepared formulations were found to be having entrapment efficiency within acceptable limits in the range of 82.16%-96.20% respectively. As the polymer i.e., stabilizer concentration increases, the drug release rate decreases, whereas Nanosuspension strength increases.

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