IJMPR 2021, 5(4), 175-180

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Research Article
SJIF Impact Factor: 5.273

REVIEW ON FORMULATION AND EVALUATION OF VERAPAMIL BY USING SOLID DISPERSION TABLETS FOR SOLUBILITY ENHANCEMENT

Manisha K. Pimpalkar*, Swapnali S. Todkar, Akshada V. Deshmukh and S. V. Patil

Students, B pharm. Final year, Ashokrao Mane Collage of Pharmacy Peth Vadgaon Maharashtra – India.

Received on: 05/06/2021
Revised on: 25/06/2021
Accepted on: 15/07/2021

***Corresponding Author**
Manisha K. Pimpalkar
Students, B Pharm. Final Year, Ashokrao Mane Collage of Pharmacy Peth Vadgaon Maharashtra – India.
manishapimpalkar076@gmail.com

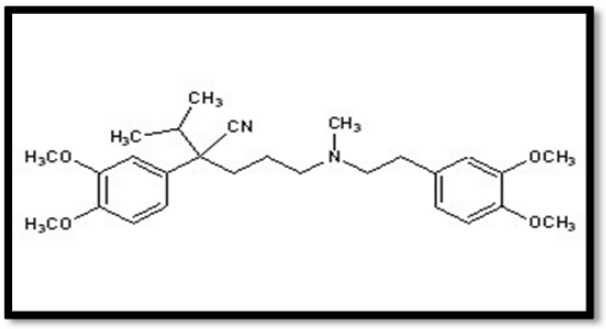
ABSTRACT

The goal of the research was to use solid- dispersion via direct compression to increase the solubility and dissolving rate of the medication Verapamil. Solid dispersions were prepared by solvent evaporation technique using PEG 6000 and Urea as carriers. Verapamil solid dispersion was developed by, melt solvent method and to modify the release and enhance solubility of the drug. The used to determine the physical state of the disseminated verapamil in the polymer matrix. By using the direct compression method, verapamil solid dispersions (FT 12) were formed into tablets. Verapamil solid dispersion dissolving was considerably improved as compared to pure drug and physical mixture. The results of this investigation convincingly showed that using water soluble carriers in various solid dispersion processes enhanced the solubility of poorly water-soluble drugs.

KEYWORDS: solid dispersion, solubility enhancement, verapamil, dissolution.

INTRODUCTION

Verapamil belongs to the calcium channel blocker class of medicines It works by relaxing blood arteries, allowing the heart to pump more efficiently. (Formula C27H38N2O4 and Molar mass 454.611 g·mol−1) To manage the heart ate, it also enhances the supply of blood and oxygen to the heart and lowers electrical activity in the heart. Verapamil is a medication that is used to treat high blood pressure. Strokes, heart attacks, and kidney issues can all be prevented by lowering blood pressure. Bioavailability 35.1% Metabolism in liver. It works by allowing blood to flow more freely by relaxing blood vessels. Verapamil is also prescribed for the treatment of chest discomfort (angina). It may aid in improving your capacity to exercise and reducing the frequency with which you get angina attacks.



Chemical structure of Verapamil

Verapamil solid dispersion was developed by kneading method, melt solvent method and co-precipitation method to modify the release and enhance solubility of the drug. On comparing with pure drug and physical mixture, the dissolution of verapamil solid dispersion was enhanced dramatically.

Definition

Solid dispersion is a term used to describe a collection of solid goods made up of at least two separate components, most commonly a hydrophilic matrix and a hydrophobic medication. Solubility is the ability of a liquid, solid, or gaseous chemical substance known as a solute to dissolve in a liquid, solid, or gaseous solvent and form a homogenous solution.

Solid dispersion (SD) has long been used to increase the rate of dissolution, solubility, and oral absorption of medicines that are weakly water soluble. SD refers to a class of solid goods that have at least two components, usually a hydrophilic matrix and a hydrophobic medicament; the matrix can be crystalline or amorphous. The solid dispersion was first used to compensate for the low bioavailability. Nearly 40% of novel chemical entities (NCEs) produced by combinatorial screening procedures with superior pharmacological activity are poorly soluble, posing a significant challenge in formulation development.

Advantages of solid dispersion

Solid dispersion is most commonly used to.

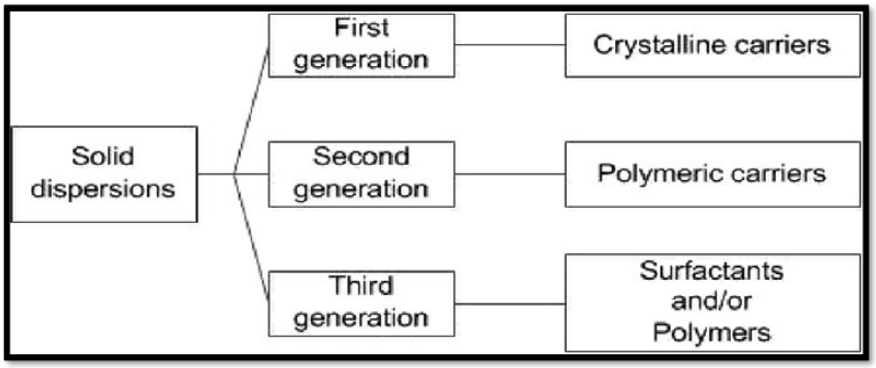
- Reduce particle size.
- To increase the drug's permeability.
- To change the drug's crystalline structure to amorphous.

- To make a poorly water-soluble medication more water-soluble. In a industry.
- To disguise the flavour of the medication.
- To achieve a uniform dispersion of a modest amount of medicines in solid state.
- For dispensing liquid or gaseous substances.
- To create a more rapid release formula In a sustained release, a priming dose is given. Dose type
- To create a long-acting or sustained-release dose.

Disadvantages of solid dispersions

- Their volatility is a significant disadvantage. They display crystallinity changes and a decrease in dissolving rate as they age.
- Temperature and moisture have a greater impact.
- The influence on solid dispersions is deteriorating. On physical concoctions
- Tackiness makes it difficult to handle.

❖ **Types of solid dispersion**



Flow chart of type of solid dispersion

❖ **Selection of carrier**

Carrier must fulfil the following characteristics.

- To be suitable for boosting a drug's dissolving rate.
- Freely soluble in water and has inherent quick dissolution qualities.
- Pharmacologically inert and non-toxic.
- For the melt process, it must be heat stable and have a low melting point.
- Passes through a vitreous condition and is soluble in a number of solvents.

❖ **Methods of solid dispersion-**

There are several methods for preparing a solid dispersion system. These techniques are listed below.

1. Melting method
2. Solvent method
3. Melting solvent method (melt evaporation)
4. Melt extrusion methods
5. Lyophilisation. techniques
6. Melt agglomeration Process
7. The use of surfactant
8. Electrospinning
9. Super Critical Fluid (SCF) technology

❖ **Evaluation of preparation of solid dispersion**

Solid dispersions were evaluated and characterized by the following methods.

Physico -chemical parameters

All solid dispersion tablet formulations and pure medication tablets had Physico-chemical properties that were confirmed to be within acceptable limits. The tablets were homogeneous in size and shape, friable, and hard enough to be useful.

1. Angle of repose

Angle of repose is important physical property used for characterization of the bulk of particulate foods and medicine such as seeds, grains, granules. The angle of repose is important for the design of processing, storage, and conveying systems of particulate materials. When the grains are smooth and rounded, the angle of repose is low. For very fine and sticky materials the angle of repose is high. Materials with low angle of repose are highly flowable and can be transported using gravitational force or a little energy.

Angle of repose ø = tan-1[h/r]

Where, h – Height of the pile in cm, r –Radius of the pile.

2. Bulk density [Db]

Bulk density is an essential parameter for process development and solid dosage manufacturing. It is used in determining the amount of powder that can fit in a space such as a blender or a hopper on a tablet press or capsule filler. It is also used to determine the amount of powder that can be fitted into a capsule

Db = M/Vb.

Where, Db – bulk density.

M - Mass of the powder,

Vb – Bulk volume of the powder.

3. Tapped density [DT]

The interparticulate interactions influencing the bulking properties of a powder are also the interactions that interfere with powder flow, a comparison of the bulk and tapped densities can give a measure of the relative importance of these interactions in a given powder

DT=M/VT

Where, DT – tapped density.
M - Mass of the powder
VT – Tapped volume of the powder.

4. Carr's index
The Carr's index (also: Carr's index or Carr's Compressibility Index) is an indication of the compressibility of a powder. The Carr's index is frequently used in pharmaceutics as an indication of the flow ability of a powder
Carr's index = Tapped density – Bulk density / Tapped density ×100

5. Hardness
Hardness is the property of a material that enables it to resist plastic deformation, penetration, indentation, and scratching. Therefore, hardness is important from an engineering standpoint because resistance to wear by either friction or erosion by steam, oil, and water generally increases with hardness.

6. Friability [F]
Friability testing is a laboratory technique used by the pharmaceutical industry to test the durability of tablets during manufacturing and distribution The result is inspected for broken tablets, and the percentage of tablet mass lost through chipping. or when a tablet has the tendency to chip, crumble or break during compression. This usually happens when the tablet is being handled, packaged or transported.
% friability = Initial weight – final weight / Initial weight ×100

7.Weight variation test
The weight variation test is to ensure - good manufacturing practices (GMP), appropriate size of the tablets and the content uniformity of the formulation. The United States Pharmacopoeia (USP) provides criteria for tablet weight variation of intact dosage units To evaluate the uniformity of dosage of pharmaceutical tablets, several samples are selected at random from the batch to be tested. Each tablet must be weighed individually and the weight recorded.

8.Dissolution testing
The measures the extent and rate of solution formation from a dosage form, such as tablet, capsule, ointment, etc. The dissolution of a drug is important for its bioavailability and therapeutic effectiveness. Dissolution and drug release are terms used interchangeably

9. Uniformity of weight
The uniformity of weight of drug is important because this ensure the even distribution of ingredients in the drug. Uneven distribution may alter the dose in each individual drug and therefore causes a lot of problems such as unable to reach the therapeutic range or exceed the therapeutic range and reach toxic range.

- **Microstructural analysis**

1. SEM Analysis
SEM (Scanning Electron Microscopy) is a test method that uses an electron beam to scan a sample and provide a magnified image for analysis. SEM analysis, often known as SEM microscopy, is a technique for microanalysis and failure analysis of solid inorganic materials that is particularly successful.

2. X-Ray Diffraction Study
The XRD technique is used to determine if a material is crystalline or amorphous. It will define how many materials are quantified. Also, studied Characterization of crystalline materials using a non-destructive method. Structures, phases, preferred crystal orientations (texture), and other structural data such as average grain size, crystallinity, strain, and crystal defects are all included.

3. Scanning Calorimetry (DSC)
DSC can be used to determine crystallinity by quantifying the heat associated with melting (fusion) of the material. DSC is a well-known technique that measures heat flow into or out of a material as a function of time or With melting (fusion) of the material. DSC is a well-known technique that measures heat flow into or out of a material as a function of time or temperature.

4.Fourier Transform Infra Red Spectroscopy (FT-IR).
FT-IR spectroscopy can be employed to find the possible interactions between the drug and the carrier in the solid state on FT-IR spectrophotometer by the conventional KBr method.

METERIALS AND METHODS

Materials
Verapamil PVPK30, β-cyclodextrin talc, magnesium stearate, ethanol, PEG6000, HPMC K100M, lactose, cross carmalose sodium.

Preparation of verapamil by using solid dispersion techniques
Solid dispersion is a common technique for enhancing the solubility of water-insoluble medications, hence enhancing their bioavailability. Solid dispersions are created using the solvent evaporation technique. In the solvent evaporation technique, the medicine and the carrier are both dissolved in a common solvent, which is then evaporated to produce solid dispersions. According to the preliminary solubility study, carriers including PEG 6000, poloxamer 188, and Urea can be utilized to improve the solubility and dissolution of solid dispersions. To improve solubility, solid dispersions are created using carriers such as PEG 6000 poloxamer and urea.

Melt Solvent Method

Melt solvent technique was used to make a solid dispersion of verapamil-PVPK30. The medication was accurately weighed and dissolved in an organic solvent before being poured into the melt of the carrier. It was suddenly cooled. The mass was placed in a desicator to dry completely. The solidified substance was crushed, pulverized, and sieved before being kept in a desicator.

Formulation table

Table no.1: Formula of Verapamil Tablets Preparation Employing Its Solid Dispersion.

Ingredients (mg)	Formulation Code												
	FTP	FT1	FT2	FT3	FT4	FT5	FT6	FT7	FT8	FT9	FT10	FT11	FT12
Verapamil	80	-	-	-	-	-	-	-	-	-	-	-	-
Solid Dispersions of Verapamil	-	163.3	246.6	322.5	164.2	243.7	321.6	165.2	250.2	322.4	166.1	252.3	323.1
Magnesium Stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Talc	7	7	7	7	7	7	7	7	7	7	7	7	7
Cross Carmallose Sodium	7	7	7	7	7	7	7	7	7	7	7	7	7
Lactose	252.5	169.2	85.90	10.50	168.3	88.80	10.90	167.3	82.3	10.10	166.4	80.20	10.30
Total Weight	350	350	350	350	350	350	350	350	350	350	350	350	350

FTP-Verapamil Pure Drug, FT1-FT3-Verapamil+PVPK30 (1:1, 1:2, 1:3), FT4-FT6-Verapamil+β-Cyclodextrin (1:1, 1:2, 1:3), FT7-FT9-Verapamil+PEG6000 (1:1, 1:2, 1:3), FT10-FT12-Verapamil+HPMC (1:1, 1:2, 1:3).

RESULTS AND DISCUSSION

Solubility study

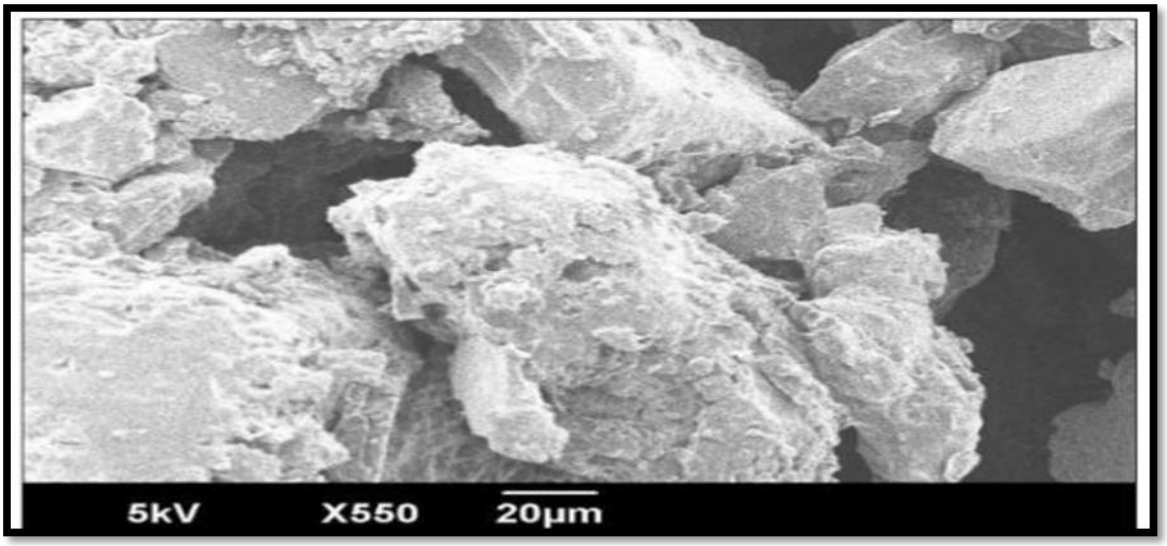
Solubility is the ability of a solid, liquid, or gaseous chemical substance (referred to as the solute) to dissolve in solvent (usually a liquid) and form a solution.

Solvent.	**Solubility**
Water.	Practically insoluble
Ethanol.	Readily soluble
Chloroform	Soluble

Characteristics

Scanning Electron Microscopy studies:

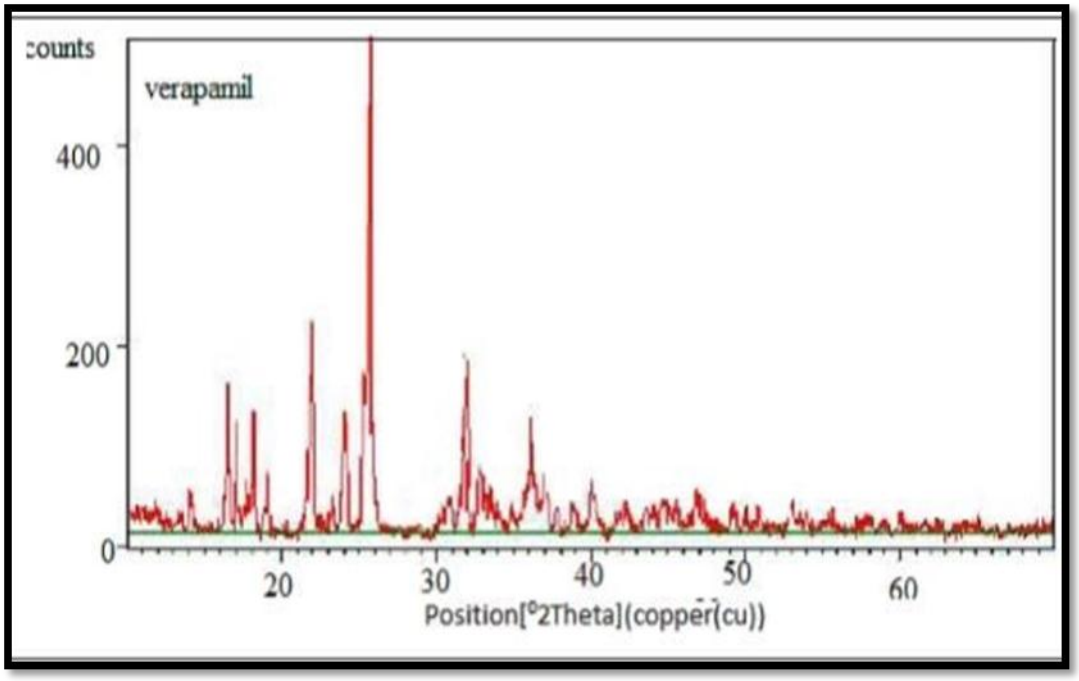
Scanning Electron Microscopy (SEM) of pure drug verapamil appeared as biconcave, irregularly flat crystals in shape are shown in figure below. Scanning Electron Microscopy of optimized batch was performed to study the surface morphology. The electron micrographs showed spherical particles in nanometer size in range.



"Fig.no 1". (SEM Image of Verapamil tablets).

XRD studies

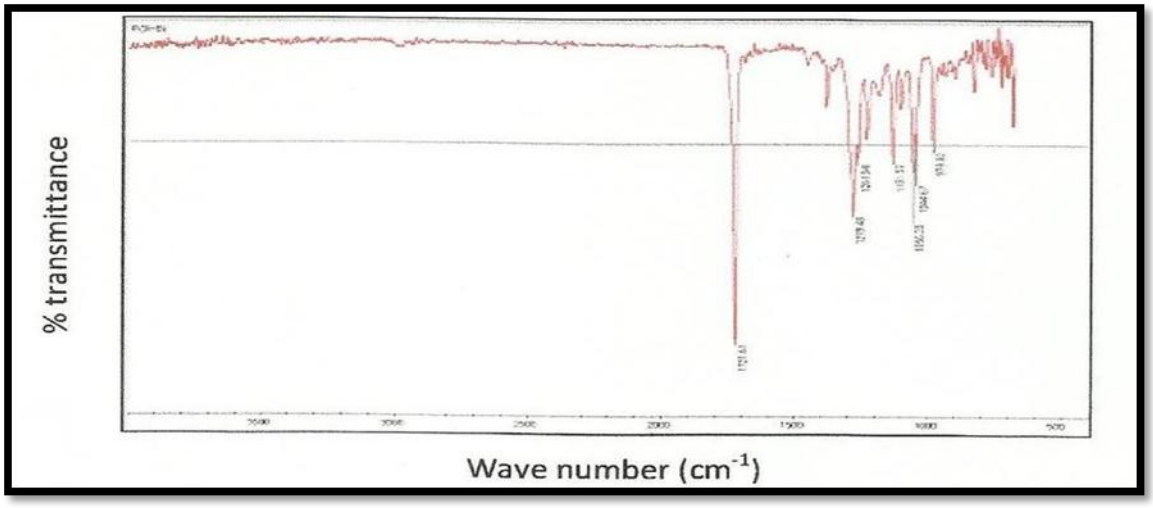
XRD pattern of Pure verapamil and XRD pattern are shown in below figures respectively. XRD pattern pure verapamil was showing sharp at 3ø-scattered angles at indicating highly crystalline nature of drug.



"Fig no 2" XRD pattern of Pure verapamil.

Fourier Transform Infrared Spectroscopy

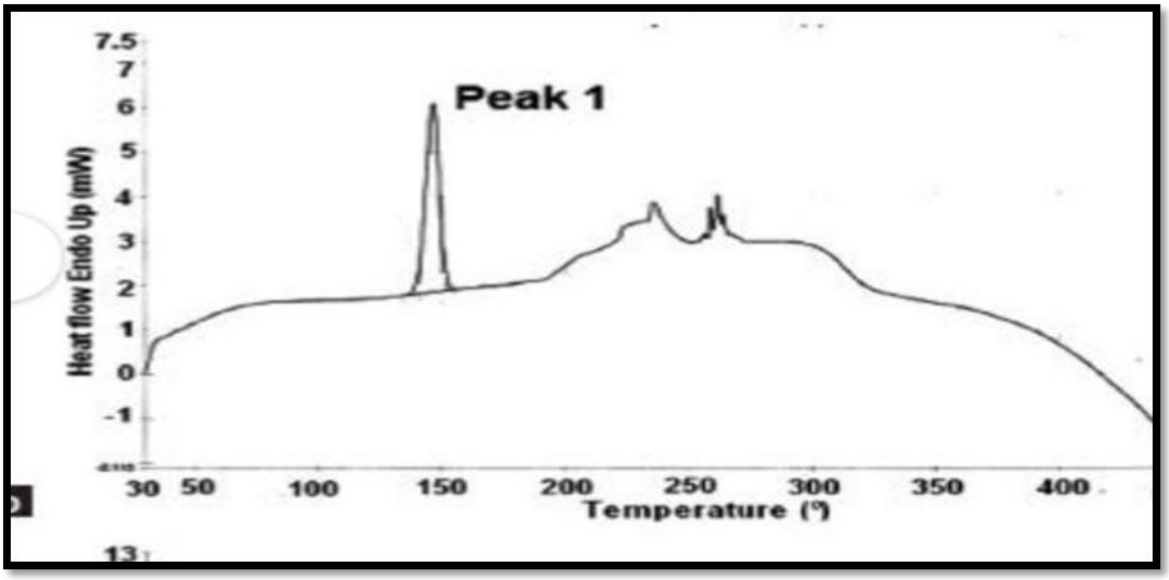
FTIR pattern of pure verapamil show the below fig . IR spectra of solid dispersions of verapamil were compared with the standard spectrum of verapamil IR spectrum of verapamil hydrochloride is characterized by the absorption of NH group at 3,467 cm.



"Fig no 3" FTIR pattern of pure verapamil.

DSC Studies

The DSC thermograms of pure verapamil showed a sharp endothermic pack at , Peak onset was 141.26º, apex 146.62ºc indicating the melting point as show in below fig DSC Studies.



"Fig no 4": The DSC thermograms of pure verapamil.

CONCLUSION

Verapamil tablets were prepared by direct compression method. The release and dissolution of drug from the tablets can be increased by formulating it as solid dispersion tablets. The formulation FS-12consists of verapamil [150mg], Poloxamer-188 [150mg], HPMC-K4M [75mg], Lactose [51mg], magnesium stearate [12mg] and talc [12mg] was selected as the optimized formulation with sufficient rate of release and in-vitro dissolution. Various physicochemical parameters tested for this formulation have shown good results. It was concluded that development of sustained release-solid dispersion tablets not only releases the drug for a sustained period of time but also increases the dissolution rate of Verapamil. In addition, these formulations reduce the need of frequent administration and enhance patient compliance.

ACKNOWLAGEMENTS

The author thanks the principal, Ashokrao Mane college of pharmacy, Peth Vadgaon for providing support and facilities during review work.

REFERENCE

1. Sameer Singh, Raviraj Singh Baghel and Lalit Yadav, "A review on solid dispersion", International Journal of Pharmacy and Life Sciences, Sep 2011; 2(9): 1078-1095.
2. Sekiguchi, and N. Obi, "Studies on absorption of eutectic mixture" I. A comparison of the behavior of eutectic mixture of sulfathiazole and that of ordinary sulfathiazole in man," Chemical and pharmaceutical bulletin, 1961; 9: 866-872.
3. L. Chiou, and S. Riegelman, "Pharmaceutical applications of solid dispersion systems," Journal of Pharmaceutical Sciences, 1971; 60(9): 1281-1302.
4. Dhirendra K, Lewis S, Udupan, et al. A Review on Solid Dispersion. Pak J Pharm Sci, Apr 2009; 22(2): 234–246p.
5. Vishal Gupta, Madan AK, Rajesh Agarwal. Rapidly Soluble Tablets through Amalgamation of Cube Sugar and Solid Dispersion Technologies. Int. J Pharm Front Res, Jul–Sep 2011; 1(2): 1–13p.
6. Singh Jaskirat, Walia Manpreet, Harikumar S L, "Solubility enhancement by solid dispersion method: A review", Journal of Drug Delivery and Therapeutics, 2013; 3(5): 148-155.
7. Anupama Kalia, Mayur Poddar, "Solid dispersions: an approach towards enhancing dissolution rate", International journal of pharmacy and pharmaceutical sciences, 2011; 3(4): 0975-1491.
8. Patel BP, Patel DM, Patel JK. A Review on Techniques which are Useful for Solubility Enhancement of Poorly Water Soluble Drugs. International Journal for Research in Management and Pharmacy (IJRMP), Dec 2012; 1(1): 56–70p.
9. Nadia Saffoon, Riaz Uddin, Naz Hasan Huda, et al. Enhancement of Oral Bioavailability and Solid Dispersion: A Review. Journal of Applied Pharmaceutical Science (JAPS), 2011; 01(07): 13–20p.
10. Hind AlZein, Khalil Sakeer, Alanazi Fars K. Designing an Extended Release Waxy Matrix Tablets Containing Nicardipine-hydroxy Propyl β Cyclodextrin. Saudi Pharm J, 2011; (19): 245–253.