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# FORMULATION AND IN-IVTRO EVALUATION OF SOLUBILITY ENHANCEMENT OF AZILSARTAN MEDOXOMIL USING NANO SUSPENSION TECHNOLOGY

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## ABSTRACT:

Poor aqueous solubility of some drug molecules is a major problem in drug formulation. Drug nano suspensions emerged as one solution to delivering such hydrophobic drugs. Scaling down to nano suspensions enhances drug aqueous solubility and bioavailability by increasing drug surface area that comes into contact with biological media. Azilsartan's oral nanosuspension was prepared using Solvent evaporation technique using different polymers like SLS, PVP-K30, poloxamer 188. For trapment efficiency, zeta potential, SEM analysis, invitro dissolution research, all the formulation was assessed. It was discovered that all the prepared formulations had trap effectiveness within acceptable boundaries of 86.36±0.54%- 96.54±0.52% respectively. Studies of IR spectroscopy showed no drug-exceptional interactions. Compared to other formulations, all F3 formulations are the finest formulations, showing 98.40 percent of the drug produced in 45 minutes respectively and following the kinetics of first order release.

Keywords: Azilsartan, PVP K30, SLS, poloxamer.

## INTRODUCTION

Drug Delivery System are getting more and more state-of-the-art as pharmaceutical scientists collect a higher information of the physicochemical and biological parameters pertinent to their performance. Despite incredible blessings in drug shipping, the oral route remains the maximum preferred course for the administration of therapeutic sellers because of the low price of therapy and ease of management leads to excessive-level of patient compliance. On the alternative hand, this excessive-throughput screening process has executed little to address the issue of poor bioavailability of orally administered drug candidates. Many national distribution schemes have been created over the previous two centuries to function as drug reservoirs from which the active

substance can be published at a predetermined and monitored pace above a precise interlude of moment.

For centuries, the electronic substance distribution scheme (oral DDS) has been regarded as the the majority worn path for drug administration among all the paths that have been studied for the systemic distribution of drugs through distinct dosage forms of pharmaceutical products. Over 50 percent of the market's drug release system are oral DDS.

**Ideal drug delivery systems with two primary characteristics:**

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**Ideal drug delivery systems with two primary characteristics:**

- A single dose should be used for the entire duration of treatment.
- The effective drug should be delivered straight at the action site.

It's hard to develop such perfect schemes. Scientists are trying to create technologies that are as near as feasible to perfect structures. Attempts to create a single dose therapy have concentrated attention on regulated or sustained release DDS for the entire length of treatment.

**Novel drug delivery system:**

The development of orally regulated DDS should focus mainly on achieving greater predictability and bioavailability. Now-a-days most pharmaceutical scientists are engaged in the development of the ideal DDS. This optimal scheme should benefit from a single dose for the entire therapy period and should produce the effective drug straight at the particular location.

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Controlled release implies the predictability and reproducibility to control the drug release, drug concentration in goal tissue and optimization of the healing impact of a drug with the aid of controlling its launch in the frame with decrease and less frequent dose[1]. However, owing to variable gastric emptying and motility, this strategy is packed with several physiological challenges such as the failure to stop and identify the controlled drug delivery scheme within the required GIT region. In addition, the comparatively short GET in animals, which usually averages 2-3 hours through the significant absorption area, i.e., the stomach and upper portion of the intestine, may lead in unfinished drug discharge from the drug delivery scheme resulting in decreased dose efficacy. Control of the positioning of a DDS in a particular region of the GIT therefore provides benefits for a multitude of significant drugs defined by a small absorption window in the GIT or stable drugs[2].

Many of the new chemical entities being created through drug discovery programmers (roughly 40 percent or more) are poorly water-soluble. The formulation of drugs that are poorly water-soluble have forever be a confront for pharmaceutical researchers[3]. The low speed of saturated solubility and dissolution results in bad bioavailability. The issue is more serious for BCS category II drugs, for instance Itraconazole and carbamazepine, because they are inadequately soluble in mutually organic and aqueous environments.[4] These medicines output is dissolution-rate-limited and is influenced by the patient's fed / fasted condition. Both the shape and the particle size are correlated with the dissolution levels of sparingly soluble drugs. Hence reduce in particle dimension consequences in augment in dissolution rate. There are quantity of components methods that may be used to solve the troubles associated with the low solubility and coffee bioavailability of sophistication II tablets. Some of the strategies to growth solubility include micronization, solubilisation the use of cosolvents, use of permeation enhancers, surfactant dispersions, salt formation and precipitation techniques[5,6]. Most of these method for ornamental solubility have both benefits and constraints and therefore have restricted usefulness in enhancing solubility. Other methods used to enhance solubility such as microspheres, emulsions, micro emulsions, liposomes, supercritical handling, strong dispersions and complexes of incorporation using cyclodextrins[7,8] .They demonstrate sensible achievement, but absence universal applicability to all drugs that are not soluble in together aqueous and organic media. Nanosuspensions have disclosed their ability to conduct issues related to the shipment of drugs that are poorly water-soluble and lipid-soluble and are special due to their simplicity and the benefitsthey confer on other approache Nanotechnology opens up new vistas of research in the improvement of novel drug delivery systems. “Nano” word comes from the Greek word‘ nanos ”which means dwarf [9]. Nano implies it's 10-9 or 1 billionth component. Nanosuspension is drug particle dispersion submicron colloidal. It is described in an aqueous car as dreadfully daintily colloid, biphasic, distributed strong medication droplets, size less than 1 μm stabilized by

surfactants and polymers prepared by appropriate medication distribution techniques. Nanosuspension has disclosed its capacity for solving the issue of delivering drugs that are poorly water-soluble and poorly water-soluble and lipid-soluble. It improves absorption and bioavailability and helps to lower the amount of standard oral dosage forms[10].

Micronization of inadequately soluble medicaments by colloid mills or jet mills has been chosen for a lengthy period of moment. The general distribution of particle volume varies from 0.1μm to about 25μm, with only a negligible quantity in the nanometer spectrum below 1μm.

When to go for Nanosuspensions Approach

- It is intended to prepare nanosuspensions for water-insoluble compounds (but oil- soluble) with a elevated log P value.
- Usually drugs that are insoluble in water but soluble in the oil phase system are developed in liposomes, emulsion structures, but these methods to lipid processing do not apply to all drugs.
- Nanosuspensions are favored in these instances. Nanosuspensions are used as a design strategy for drugs that are insoluble in both water and organic media instead of using lipidic structures.
- The nanosuspension design method is best suited for compounds of elevated log P value, elevated melting point and elevated dose[11, 12]

Depending on the manufacturing method, modifications may happen in the drug particle's crystalline structure. An rise in the amorphous drug percentage could lead to greater solubility in saturation. Nanosuspension not only solves the issue of bad solubility and bad bioavailability, it also alters the drug's pharmacokinetics and enhances drug safety and effectiveness

**Advantages:**

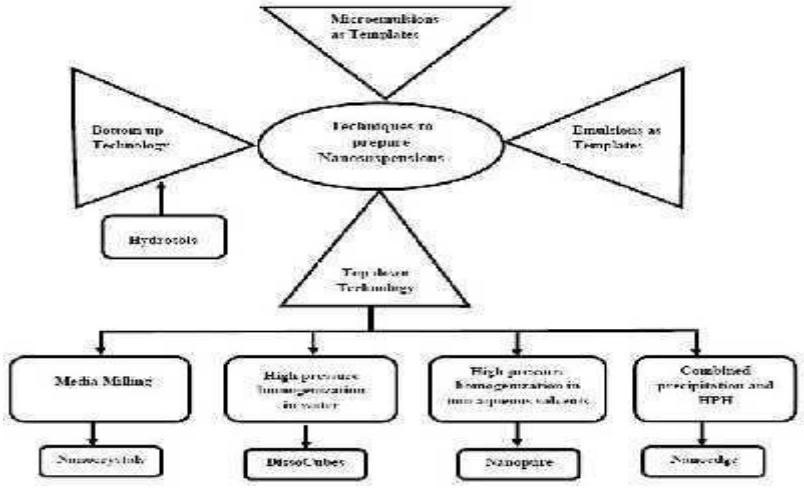
- Most price efficient.
- Useful for drugs that are not very soluble.
- More stable physically than liposomes.
- Provide manufacturing facility and scale up for manufacturing on a big scale.
- Rapid targeted dissolution and tissue.
- Reduction of inflammation of the tissue.
- Higher bioavailability in drug delivery in the eyes and inhalation.

**Potential Benefits of Nano suspension Technology for Poorly Soluble Drugs:**

- Reduced particle size, enhanced medication dissolution frequency, enhanced intake frequency and magnitude, enhanced medication bioavailability, plasma vs. time curve, start-up moment, medication maximum, decreased variation, decreased fed / fasted results.
- For compounds that are water-insoluble but soluble in oil, nanosuspensions can be used. In comparison to lipidic structures, on the other side, nanosuspensions can be used to formulate compounds that are insoluble in both water and oils.
- Nanoparticles may attach to the mucosa of the gastrointestinal tract, prolonging the

drug's contact period and thereby increasing its absorption.

- A significant benefit of nanosuspension is that there are many paths of nanosuspensio n administration, such as oral, parenteral, respiratory, dermal and ocular.




Nano-suspension of nanoparticles (NPs) provides numerous benefits over standard ocular dosage forms, including decrease of dose levels, retention of drug discharge over an extended period of moment, decrease of internal toxicity of the drug, increased drug absorption owing to shorter residence time of nanoparticles on the corneal surface, greater levels of drugs in the affected tissue,

- Nanosuspension has small prevalence of exceptional side impacts.

Nanosuspensions solve compound shipping problems by avoiding the need to dissolve compounds and by keeping the drug in a desired crystalline state of sufficient Size for pharmaceutical acceptance.

- Increased hydrolysis and oxidation resistance, enhanced resting physical strength.
- Reduced amounts of administration; vital for intramuscular, subcutaneous and ophthalmic use.

*Finally, Nanosuspensions can provide the passive targeting10-15*

**PREPARATION TECHNIQUE OF NANOSUSPENSION[10-15]**

There are mainly two techniques for nanosuspension preparing.

The traditional precipitation strategies (hydrosols) are known as "bottom-up method." In Bottom up Technology the drug is dissolved in a solvent, that is then introduced to non-solvent to precipitate the crystals. This technique is that in the precipitation process the developing of the drug crystals desires to be controlled by using addition of surfactant to keep away from formation of microparticles. The "Top down Technologies" consists of Media Milling (Nanocrystals), High Pressure Homogenization in Water (Dissocubes), High Pressure Homogenization in Non-Aqueous Media (Nanopure) and High Pressure Homogenization (Nanoedege).

*Figure No 1: Various methods for*

**Homogenization in Water (Dissocubes):**

Dissocubes technology was developed by uller in 1999. With pressures from 100 –1500 bar (2800–21300 psi) and up to 2000 bars (for laboratory scale), the device can be used. To prevent

the blocking of the homogenization gap, the micronized drug particle size must begin with less than 25 μm. Therefore, a pre suspension of micronized drug with surfactant solution is required using high speed stirrer. For this reason, it should be necessary to prepare.

**Principle:**

The decrease of the piston gap is base on the principle of cavitation. Particles are reduced also as a consequence of elevated clip forces and particle collisions. The dispersion is within a cylinder of 3 cm in diameter; suddenly a very narrow gap of 25μm is reached. The flow volume of liquid by transverse section within a closed system is constant under Bernoulli's Law. The 3 cm to 25 μm reduction in diameter increases dynamic pressure and decreases static pressures underneath the boiling point at room temperature. As a outcome of this water, the sweltering at room warmth starts and the gas bubbles are formed that implode whilst the deferral leaves the slit and the normal air pressure. The size of the medicine nanocrystals to be obtained depends mainly on factors such as temperature, number of cycles of homogenization and homogenizer power density.

The suspension in this technique is forced into a narrow valve under a high pressure by a pressure plunger pump (Figure 3). The static pressure is reduced to below the burning water pressure, which results in boiling water and the formation of gas bubbles if the suspension is allowed through the hole. When the opening pressure leaves, the bubbles will implode. This causes a shrinkage of the surrounding particles to rush onto the surface. This principle is engaged in apv gaulin micron lab 40 homogenizer.

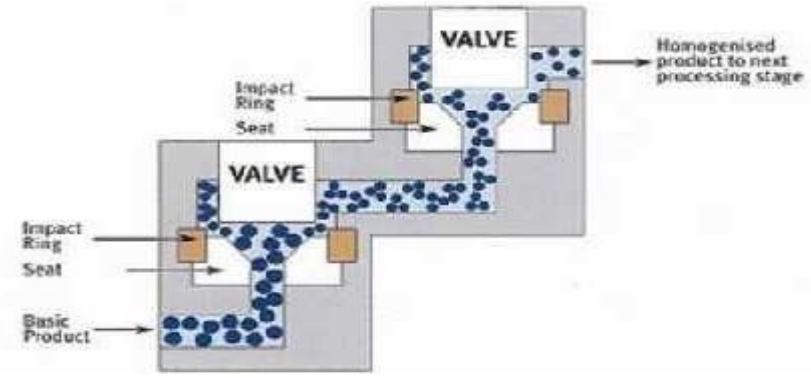



Figure No 2: High pressure homogenization

**Advantages:**

- The erosion of processed materials is not caused.
- It applies in both water and organic media to medicines which are poorly soluble.
- The aseptic production for parental administration of nanosuspensions is permitted.

**Disadvantages:**

- Pre-processing such as drug micronization is necessary.
- The cost of the dosage form is increased by the use of high cost instruments.

**Homogenization in Non aqueous Media (Nanopure):**

Synthetically unstable medications can be prepared in nonaqueous or water miscible fluids alongside polyethyleneglycol-400 (PEG), PEG1000, etc. At room temperatures, 0oC and underneath cooler (-20oC), the homogenization can be practiced.

**Combined Precipitation and Homogenization (Nanoedege):**

Crystal growth in the size of microcristals tends to continue with precipitated medicament nano-particles. They must be processed with high power (homogenisation). They are in totally indistinct, mostly formless or totally crystalline which make issues in long haul strength just as in bioavailability, so the encouraged molecule suspension is along these lines homogenized which safeguard the molecule size got after the precipitation step.

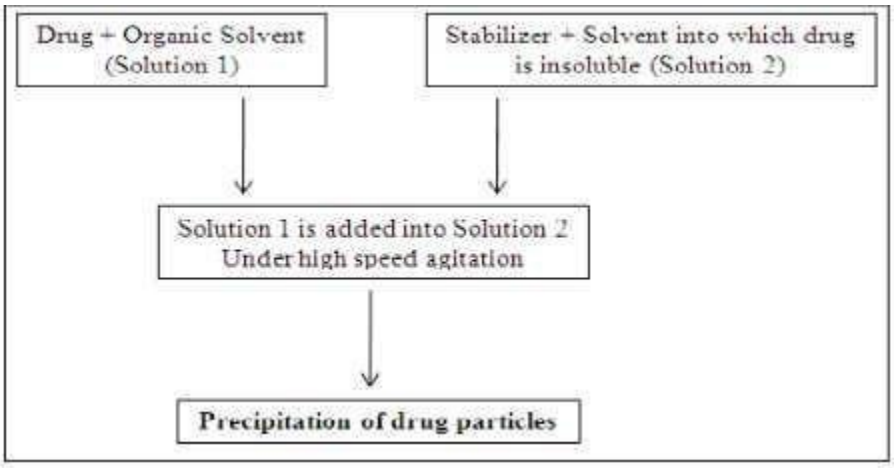



Figure No 3: Method for preparation of nanoedge

**Precipitation technique (solvent-anti solvent method):**

The precipitation technique for getting ready submicron particles has been utilized for a long time. It is utilized essentially for low-solvency meds. First medication is broken down in a reasonable dissolvable. This arrangement is then blended with a miscible antisolvent framework within the sight of surfactants. Quick expansion of medication arrangement in to the antisolvent prompts the unexpected super immersion of medication in the blended arrangement structures ultrafine sedate solids. Precipitation strategy includes two stages cores arrangement and precious stone development. A high nucleation rate and a low development rate are important to set up a steady suspension with the base molecule size. The two rates are temperature-subordinate. The medication must be dissolvable in at any rate one dissolvable in this system, which is miscible with non-dissolvable.

**Nanojet technology:**

This method is likewise alluded to as the contrary stream innovations, which utilize a chamber where a suspension stream is partitioned into at least two sections. During the procedure, high shear power lead to a decrease in molecule size. Nanosuspensions of atovaquone had been set up by Dearns utilizing a

smaller scale fluidizer. The significant weakness of this strategy is the high number of goes through the small scale fluidizer and that the item got contains a generally bigger portion of microparticles.

**Supercritical fluid methods:**

Nanoparticles are delivered utilizing various techniques, for example, fast development of the supercritical arrangements (RESS), the supercritical antisolvent strategy and PCA precipitation. With the RESS system, the medication arrangement has been ventured into supercritical liquid by a spout, which causes the precipitation of the medication as fine particles by the loss of supercritical liquid dissolvable power. By utilizing RESS technique, Young et al. arranged cyclosporine nanoparticles having distance across of 400 to 700 nm. In the PCA strategy, the medication arrangement is atomized into the CO2compressed chamber. The arrangement will be supersaturated when the dissolvable is evacuated and precipitation will in the end occur. In the supercritical enemy of dissolvable procedure, tranquilize arrangement is embedded and the dissolvable is removed, and the medicine arrangement is super-immersed.

Lipid Emulsion/Microemulsion Template: The emulsion shaped in a customary procedure utilizing the somewhat miscible water dissolvable as a scattered stage is another approach to create nanosuspensions. The weakening of the emulsion just outcomes in nanosuspensions. Besides, microemulsions as formats can deliver nanosuspensions. Smaller scale emulsions are thermodynamically steady and isotropically clear scatterings of two immiscible fluids, for example, oil and water balanced out by an interfacial film of surfactant and co-surfactant. The medication can be either stacked into the inward stage or the preformed smaller scale emulsion can be immersed with the medication by close blending. The medication Nanosuspension brings about proper microemulsion weakening. A case of this is the nanosuspension of griseofulvin, which is created with water, butyl lactate, lecithin and taurodeoxycholate sodium salt utilizing the microemulsion strategy.

The benefits of lipid emulsions as layouts for nanosuspension development are that they simple to create by controlling the emulsion bead and simple for scale-up. Be that as it may, the utilization of natural solvents influences the earth and a lot of surfactant or stabilizer are required

**Criteria for selection of drug for Nanosuspensions:**

The API with moreover of the subsequent individuality is prepared for nanosuspension. In water and oils the water is insoluble but soluble in oils (High Log P) or APIs. Drugs with reduced crystal tendance to dissolve, with a very large dose, irrespective of the solvent API.

**APPLICATIONS OF NANOSUSPENSIONS:**

**Oral Drug Delivery:**

During oral administration of antibiotics, such as bupravaquone and bupravaquone, many of the medicinal substances (figures) have a number of advantageous oral routes

By nanosize it will become more soluble and more bioavailable.

Figure No 4: Nanosuspensions for Oral Drug Delivery

**PREPARATION OF CALIBRATION CURVE OF AZILSARTAN**

**Procedure for standard curve in pH 6.8:**

10 mg of Azilsartan was dissolved in 10 ml of pH 6.8 by slight shaking (1000 µg/ml). 1 ml of this solution was taken and adjusted to 10 ml with pH 6.8, which gives 100 µg/ml concentration (stock solution). From the stock solution, concentrations of 2 , 4 , 6 , 8, 10 and 1 2 µg/ml in pH 6.8 were prepared. The absorbance of diluted solutions was measured at 231nm and a standard plot was drawn using the data obtained.

**Method of Preparation Nanosuspension:**[30-]

**Solvent evaporation method:**

At room temperature (organic phase), Azilsartan was dissolved in methanol. It was poured into water with various PVP K30 stabilizer, Polaxomer 188 and SLS, which was maintain at room warmth and then stirred in magnetic stirrer, stirred for thirty minutes at rpm 800-1000, to evaporate the volatil solvent. A syringe placed directly into a stabilizer containing water is used to add organic solvents. Organic solvents evaporated at a 1 hour room temperature and then sunken for 1 hour under a sluggish alluring emotive of the Nanosuspensions

| **Ingredients** | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
|---|---|---|---|---|---|---|---|---|---|
| Azilsartan | 320 | 320 | 320 | 320 | 320 | 320 | 320 | 320 | 320 |
| SLS (mg) | 60 | 120 | 180 | -- | -- | -- | -- | -- | -- |
| PVP K30(mg) | -- | -- | -- | 60 | 120 | 180 | -- | -- | -- |
| Polaxomer 188 | -- | -- | -- | -- | -- | -- | 60 | 120 | 180 |
| Methanol (ml) | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Water (ml) | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |

**Table No 1 Formulation of nano suspensions**

**Evaluation parameters of Nanosuspension Azilsartan:**[34-39]

**Entrapment efficacy:** A cool ultracentrifugal system centrifuged the recently equipped nanosuspension at 20k rpm for 20 min at 5 ° C temprature. The amount of unincorporated medication was determined by the use of an UV spectrophotometer to control blank / nanosuspension absorbing the appropriately diluted 5 ml supernatant solution at 231 nm. The DEE was premeditated by removing from the preliminary quantity of medicine the sum of gratis medicine in the supernatant.

$$\%\text{Entrapment efficiency} = \frac{\text{Drug content}}{\text{Drug added in each formulation}} * 100$$

**Scanning electron microscopy**: Scan electron microscopy at different magnifications show the morphology features of Azilsartan nanosuspension.

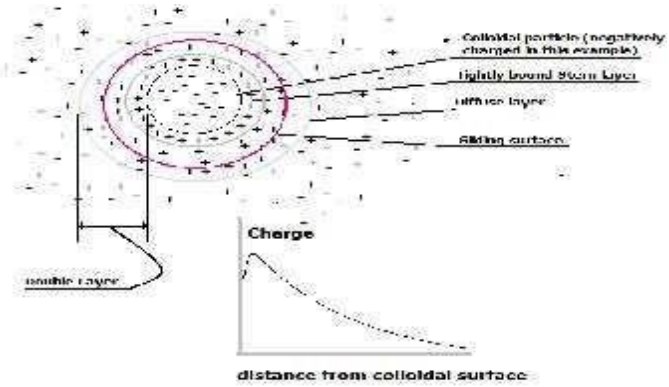
**Particle size and shape**

Malvern Zetasizer ZS was used as a medium for the average particulate size and form of the formulated nanosuspension. The sample was 100 times scanned for particle size determination.

**Zeta potential:**

There are three ways to get a surface charge from a solid particle (colloid) scattered in a liquid medium. First of all, the ions in the solution are adsorbed. Second, by the ionization of functional groups on the particle's surface. Third, due to the difference in dielectric constant between the particle and the medium. Attention should be paid to the formation of electric double layer at the solid-liquid interface. The zeta Potential is characterized as the distinction in potential between the outside of the firmly bound layer (shear plane) and the electro-impartial district of the arrangement. The potential step by step diminishes as the good ways from the surface increments.

**Figure No 5: Schematic of the formation of electric double layer.**




The zeta potential falls quickly as the electrolyte concentration increases in the medium due to the counter-ion screening effect (Figure). However, it can be computed with theoretical

models and experimentally determined electrophoretic movement data. The zeta potential can not be measured directly. The theory is based on electrophoresis and can be expressed as:

$$\mu = \zeta\varepsilon/\eta$$

Where (μ) is the electrophoretic mobility, (ε) is the electric permittivity of the liquid, (η) Is the viscosity and (ζ) us the zeta potential.

## RESULTS & DISCUSSION

### Determination of melting point

Azilsartan melting point was determined to be 212ºC by capillary method.

### Saturation Solubility

Saturation solubility was carried out at $25^0$C using 0.1N HCL, 6.8 phosphate buffer, and other solvents.

**Table No 2 : Solubility data:**

| | Media | Solubility(mg/ml) |
|---|---|---|
| **Solubility data:** | 0.1N HCL | 0.568 |
| | Ethanol | 0.985 |
| | Methanol | 1.263 |
| | pH 6.8 phosphate buffer | 0.923 |
| | pH 7.4 phosphate buffer | 0.754 |

**Discussion:** From the above solubility studies conformed that pH 6.8 phosphate buffer has greater solubility when compared with other buffers and methanol shows greater solubility than ethanol.

**Determination of absorption maximum (λmax):**

**Table No 3: Standard graph of Azilsartan in pH 6.8 (λmax 231nm)**

| Concentration (µg/ml) | Absorbance |
|---|---|
| 0 | 0 |
| 2 | 0.109 |

| | |
|---|---|
| 4 | 0.207 |
| 6 | 0.298 |
| 8 | 0.402 |
| 10 | 0.493 |
| 12 | 0.604 |

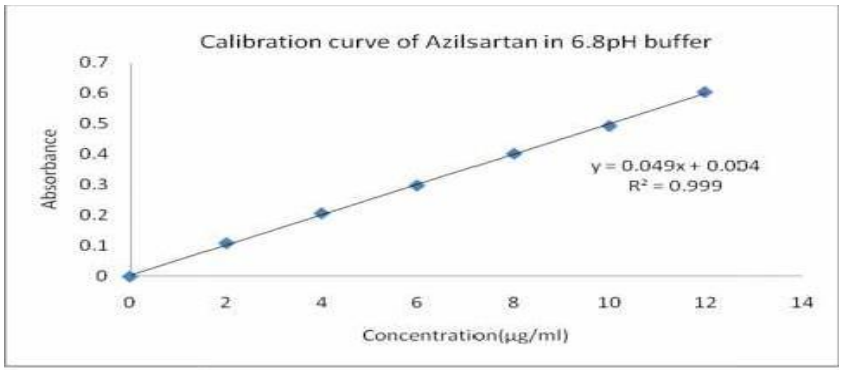



**Figure No 5**: **Standard calibration curve of Azilsartan in pH 6.8**

**Drug excipient compatibility:**

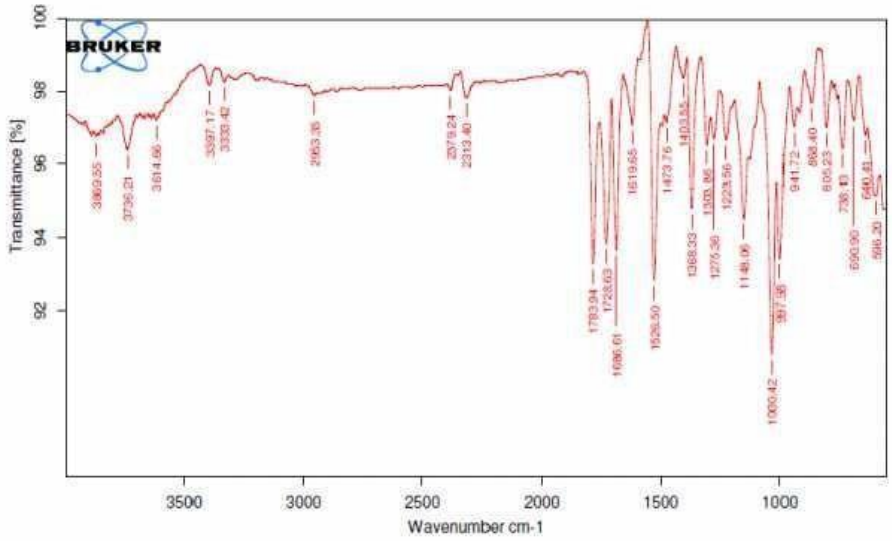



**Figure No 6: IR spectrum of Azilsartan**

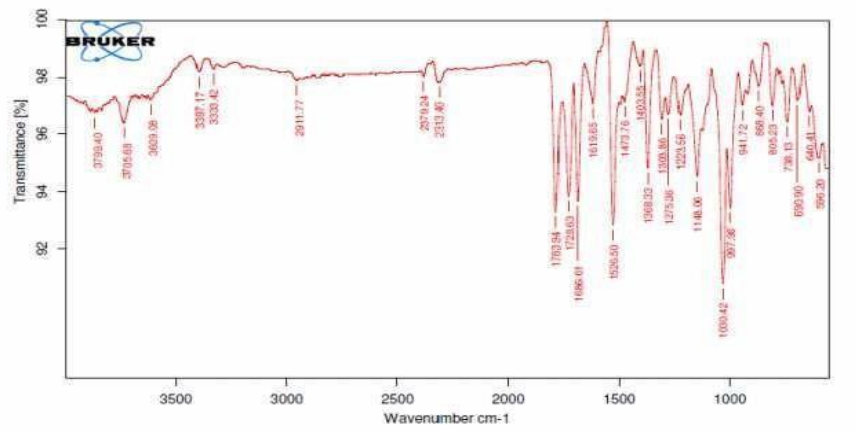



**Figure no 6: IR spectrum of Azilsartan Optimized Formulation**

**Discussion:** We observe forms of drug compatibility studies that no

## SUMMARY & CONCLUSION

An angiotensin II anthrax is used to treat serene to sensible vital hypertension by Azilsartan medoxomil. By enhancing its dissolution, the effectiveness of Azilsartan can be improved. Reducing the particle size to nanoscale can assist the surface area boost to improve formation. It can be developed as a nanosuspension because of its elevated half-life. Nanosuspension is a novel method used to progress drug solubiltty by solvent evaporation. The Nano suspensions represent a new, promising target and controlled dosage form, important for the easy production and diversified applications. The current tendency is that biodegradable polymer is used because of its accessibility and low toxicity in pharmaceutical research. The technique of solvent evaporation using SLS,, Polaxomer, PVP K30 and methanol was worn to produce the drug-containing nanosuspension as organic solvents.

In this study the solvent evaporation technique is worn to develope nanosuspension. The Nano suspensions are a successful new destination and regulated released dosage, which is increasingly important due to the ease of production and the wide range of apps. The current trend in pharmaceutical research is the use, thanks to its accessibility and small toxicity, of biodegradenable polymer. Drug-containing nanosuspension has been formulated using a technique of solvent development using SLS, Polaxomer, PVP-K30, and methanol mixes and adequate water quantities. Spectrophotometrically at 231 nm, an estimate of Azilsartan was carried out.

For parameters such as entrapement effectiveness, electron scanning, particle size testing, in-vitro discharge possibilities, interactions between drug excipients (FTIR), Nanosuspension was assessed. The MP of Azilsartan was determined by capillary technique in the assortment of 212 ° C. The trapping effectiveness was discovered to be 86.36±0.54%- 96.54±0.52% respectively, of the designed Nanosuspension. The zeta value was discovered to be within reasonable boundaries of the optimized formulation (F3). The average particle size of the optimized formulations nanosuspension (F3) was 179.5nm. The in vitro research indicate that F3 is the finest method to deliver 98.40 percent of the medications within 45 minutes when all other formulations need 45-60 minutes to discharge the medicine. The release of the medication from the Nanosuspension was

clarified by the first order of first order, by mathematical model equations. Due to regression scores the optimized formula F3 has been found following kinetics of the first ord

**REFERENCES**


1. Chen J, Park H, Park K. Synthesis of superporous hydrogels: fast swelling hydroge ls and superabsorbent properties. J.Biomed.Mater.Res.1999; 44(1):53-62.
2. Chingunpituk, J., Nanosuspension technology for drug delivery. WJST. 2007; 4:139–153.
3. Wong S.M, Kellaway I.W, Murdan S. Improved dissolution rate and oral absorption of a poorly water-soluble drug by the formation of a surfactant containing micro-particles. International Journal of Pharmaceutics. 2006; 317: 61- 68.
4. Parikh R.K.,Manusun SN.S.,Gohel M.C. and Soniwala M.M. Nimesulide enhancement dissolution using complexing and salt formation techniques. Indian drugs. 2005; 42(3):149-154.
5. Rao GCS, Kumar MS, Mathivanam N, Rao MEB. Advances in Nanoparticulate Drug Delivery Systems. Indian Drugs, 2004; 41(7): 389-395.
6. Velmula M, Pavuluri P, Rajashekar S, Dr. Rao VUM. Nanosuspension Technology for Poorly Soluble Drugs - A Review. WJPPS 2015; 4(7):01612-1625.
7. Mohanty S, Role of Nanoparticles in Drug Delivery System, Int. j. pharm. biomed., 2010; 1 (2): 41-66.
8. Ch.P .A Review on Nanosuspensions In Drug Delivery, IJPBS,2011; 2: 549-558.
9. Nagare SK, A review on Nanosuspension: An innovative acceptable approach in novel delivery system, UJP, 2012; 1(1):19-31.
10. Debjit B, Nanosuspension -A Novel Approaches in Drug Delivery System. The JPI, 2012; 1(12):50-63.
11. Kamble VA, Nanosuspension A Novel Drug Delivery System, IJPBS, 2010; 1:352- 360.
12. Yadav GV, Singh SR. Nanosuspension: A Promising Drug Delivery System. An International Research Journal- Pharmacophore 2012; 3 (5): 217-243.
13. Patravale VB, Abhijit AD and Kulkarni RM. Nanosuspensions: a promising drug delivery strategy. J.Pharm.Pharcol, 2004; 5(6): 827-840.
14. Keck MC, Muller RH. Drug nanocrystals of poorly soluble drugs produced by high- pressure homogenisation. Eur. J. Pharm.Biopharm,2006; 6(2):3–16.
15. Kavitha V.B, Neethu C.S, Dinesh KB, Krishna KK, John A. Nanosuspension Formulation: An Improved Drug Delivery System. Nanoscience and Nanotechnology: An International Journal, 2014; 4(1): 1-5.
16. Bhupesh K. Ahuja, Sunil K. Jena, Sharan K. Paidi , Sarasija Suresh. Formulation, optimization and in vitro–in vivo evaluation of febuxostat nanosuspension. International Journal of Pharmaceutics, 478(2), 540-552, 2015.
17. Chaudhari Bharat.et.al.,Preparation And Evaluation Of Nanosuspension Of Poorly Soluble Drug Albendazole, Journal of Drug Discovery and Therapeutics 1 (1) 2013, 37-42.
18. Mahboob.et.al.,Formulation and Evaluation of Nanosuspension of Albendazole for Dissolution

Enhancement,Nanoscience and Nanotechnology Letters, Volume 5, Number 9, September 2013, pp. 1024-1029(6).

19. Obeidat WM, Sallam AS, Evaluation of Tadalafil Nanosuspensions and Their PEG Solid Dispersion Matrices for Enhancing Its Dissolution Properties, AAPS pharmscitech 2014 Apr; 15(2): 364–374.