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"A Review on Solubility Enhancement of Poorly Water Soluble Drug by Solid Dispersion Technique"

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Abstract— Atorvastatin calcium (ATC) is an oral anticholesteremic operator. ATC has a place to BCS class II medicate having high porousness however low watery solubility. Keeping in mind the end goal to get valuable helpful impacts, its water solubility needs to be expanded. In the present examination, endeavor was made to progress solubility and dissolution rate of ATC by planning it into solid dispersion utilizing characteristic polymer maltose monohydrate as a profoundly water dissolvable bearer. Three strategies were utilized for getting ready solid dispersion, to be specific, physical mixture, kneading and dissolvable dissipation strategy in 1:1, 1:2 and 1:3 drugcarrier proportions. The FTIR investigation of ATC, its mix with the bearer, and of the sold dispersion showed no communication between medication, bearer and other excipients utilized. The readied solid dispersion demonstrated enhanced solubility and dissolution rate when contrasted with unadulterated medication. The change in solubility might be credited to the enhanced wettability of ATC because of uniform dispersion into the transporter. The improved batch was K2, which was readied by working technique in 1:3 proportions. The improved batch discharged 99.59 % sedate inside 60 min and had solubility very nearly five folds higher than unadulterated ATC.

From the solubility esteems plainly plying strategy was more appropriate than the other two techniques utilized for getting ready solid dispersion. The XRD contemplates uncovered that the crystalline idea of ATC was lessened when defined into solid dispersion. The enhanced batch of solid dispersion was decided for defining quick discharge tablet into three batches by coordinate pressure technique by shifting the centralization of superdisintegrant, crosscarmellose sodium. Tablet arranged with 20% cross carmellose sodium indicated 99.41% medication discharge in 60 min, this medication discharge was higher contrasted with the other two batches of tablet arranged..

Keywords— Atorvastatin calcium (ATC), Maltose monohydrate, Solid dispersion, Solubility and Dissolution.

I. INTRODUCTION

Together with the porousness, the solubility conduct of a medication is a key determinant of its oral bioavailability. There have been constantly sure medications for which solubility has displayed a test to the improvement of a reasonable plan for oral organization. Illustrations, for example, griseo fulvin, digoxin, phenytoin, sulphathiazole and chloramphenicol come quickly to mind. With the ongoing approach of high throughput screening of potential remedial operators, the quantity of inadequately dissolvable medication candidates has risen strongly and the definition of ineffectively solvent mixes for oral conveyance currently exhibits a standout amongst the most continuous and most prominent difficulties to definition researchers in the Pharmaceutical industry. Oral bioavailability of medications is influenced by an assortment of elements which impact their assimilation from the gastrointestinal tract. One determinant factor for ingestion is medicate dissolution which is impacted by the solubility of the medication in the gastrointestinal fluids.

The BCS is a logical system for grouping a medication substance in light of its fluid solubility and intestinal porousness. At the point when joined with the in-vitro dissolution qualities of the medication item, the BCS considers three noteworthy factors: solubility, intestinal porousness and dissolution rate, all of which administer the

rate and degree of oral medication retention from solid oral-measurement shapes. It groups drugs into four classes as appeared in table 1.

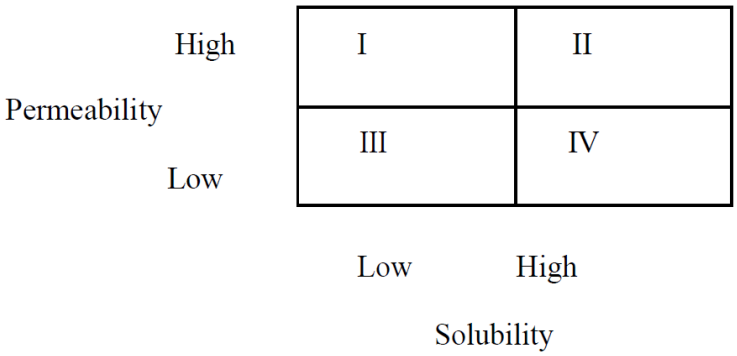


Table.1 Biopharmaceutical Classification System

Ineffectively water-dissolvable medication candidates frequently rise up out of contemporary medication disclosure projects and present formulators with significant specialized difficulties. The poor solubility and low dissolution rate of ineffectively water solvent medications in the watery gastro-intestinal liquids regularly cause inadequate bioavailability. Particularly for class II substances as indicated by the Bio pharmaceutics Classification System (BCS), the bioavailability might be upgraded by expanding the solubility and dissolution rate of the medication in the gastro-intestinal fluids.

Ineffectively water-solvent medications frequently require high dosages with a specific end goal to reach helpful plasma fixations after oral organization. Change in the degree and rate of dissolution is exceedingly alluring for such mixes, as this can prompt an expanded and more reproducible oral bioavailability and along these lines to clinically significant measurement lessening and more solid therapy.

The term solid dispersion has been used to depict a group of measurement shapes where by the medication is scattered in an organically idle network, for the most part with a view to upgrading oral bioavailability. All the more particularly, Chiou and Riegelman (1971), in their exemplary audit, characterized these frameworks as „the dispersion of at least one dynamic fixings in a latent transporter lattice at solid-state arranged by the liquefying (combination), dissolvable or liquefying dissolvable technique, while Corrigan (1985) proposed the definition just like an, item shaped by changing over a liquid medication transporter blend to the solid state.

Meaning of Solid Dispersion- Chiou and Riegelman, 1971 characterized the term solid dispersion as "A dispersion

of at least one dynamic fixings in an idle bearer or network at solid state arranged by the liquefying (combination), dissolvable or softening dissolvable strategy". Dispersions got through the combination procedure are frequently called dissolves and those acquired by the dissolvable strategy are habitually alluded to as co-accelerates or co-dissipates, for instance, Sulfathiazole-Povidone (PVP) and Reserpine-Povidone.7 There are a few medications whose solubility is improved by utilizing solid dispersion like Mifepristone8, Dyhdroartemisinin, Furosemide10, Piroxicam11 and others.

II. LITERATURE REVIEW

D. Lipinski et al…(2015), aimed to improve solubility and dissolution rate of poorly water soluble drug Atorvastatin calcium by solid dispersion technique using polymer complexation with maltose monohydrate by solvent evaporation method. Here, maltose monohydrate proved a better stabilizing agent that buffering agent.

S. S. Shinde et al...(2014), prepared the solid dispersion of Atorvastatin calcium using polymerPVP K -30 by the spray drying and solvent evaporation method. The prepared solid dispersion were characterized by IR, DSC, XRD were performed to identify the physicochemical interaction between drug and carrier. hence,its effect on dissolution of Atorvastatin improved significantly in solid dispersion technique.

A. P. Kumar et al...(2014), prepared the solid dispersion of Finofibrate by fluid – bed coater granulator using hydrophilic polymer PEG6000, surfactant,PEG400, cremophore EL, miglol and solvents IPA, DCM. prepared by solvent evaporation method.

V. Gadade et al… (2013), aimed to improve the solubility and/or dissolution rate of Atorvastatin calcium through solid dispersion using hydrophilic carriers PEG6000 and Gelucire 50/13 prepared by physical mixture and fusion method in various ratio. This study indicate potential increases in solubility and in-vitro drug release of poor water soluble drug like Acyclovir.

G. M. Khan et al… (2013), prepared the solid dispersion of Ibuprofen using glucosamine HCL by using the physical mixtures and solvent evaporation method. All solid dispersion of Ibuprofen and Glucosamine showed considerably higher.

C. Nageshetal...(2011), attempt to enhance solubility and dissolution of Fenbendazole by solid dispersion consisting of the binary and ternary system were using various+hydrophilic polymers like PVP K -25, Betacyclodextrine, Mannitol and Urea .prepared by Kneading method. The results confirmed that ternary system showed better solubility and dissolution characteristics when compared to binary system.

S. Bhise et al….(2011), aimed to improve the solubility of the poorly water soluble drug Telmisartan by solid dispersion using polymer like Gelucire 43/01, Poloxamer 407, PVP K-30 ,HPMC E4 and PEG 6000 were prepared by fusion method. All the polymer were found to be effective in increasing the dissolution rate of Telmisartan in solid dispersion when compared to pure drug.

G.V.Shavietal…(2010), aimed to improve the solubility and/or dissolution rate of Gliclazide through solid dispersion using different water soluble polymers such as PEG4000 and PEG 6000andPVP K-30 by solvent evaporation method. Solid dispersion is an effective technique in increases solubility dissolution rate and bioavailability of poorly water soluble drug.30

T.Pateletal…(2010), prepared the solid dispersion of Finofibrate using freeze drying using PEG6000, Poloxamer 407 and mixture of PEG6000 and Poloxamer 407 and comparewithother method such as physical mixture, fusion method and solvent Evaporation. Md.S.Islametal…(2010), prepared solid dispersion of Ibuprofen and Finofibrate using Poloxamer407 and Poloxamer407 micro by physical mixing technique.

S.Biswaletal...(2009), investigated the effect of the higher molecular weight PEG 8000 on the dissolution rate of Gliclazide-PEG 8000 solid dispersion and also the interaction between drug and polymer in both solid and solution state were investigated.

S. Rajarajanet al… (2009), formulated and investigate the feasibility to enhance the dissolution rate of Itraconazole by using solid dispersion.

M.V.Nagabhushanametal…(2009), formulated tablet of solid dispersion of Celecoxib employing super disintegrant and compared it with the conventional tablet.

G. Chaulangetal... (2008), evaluated the potential of the solid dispersion technique for the development of fast dissolving tablet of Furosimide with Crosspovidone as a hydrophilic carrier.

III. OBJECTVE & PLAN OF WORK

1. Need

Solubility of a drug is an important molecular property that mainly influences the extent of dissolution. Poor aqueous solubility is a very challenging problem in drug formulation development. Due to poor aqueous solubility of many drug candidates, became unsuccessful to reach the market although exhibiting potential pharmacodynamic property. It is very useful to find appropriate formulation approaches to improve aqueous solubility and thus dissolution of poorly soluble drugs. Atorvastatin calcium is the drug of choice for solubility enhancement using polymers such as maltose monohydrate. Thus improvement of solubility and dissolution of Atorvastatin calcium from its dosage form is an important issue.

2. Objective

The objective of proposed research work is to enhance the solubility and dissolution rate of Atorvastatin calcium using maltose monohydrate.

3. Plan of Work

1. The plan of work will be as follows-
2. Selection of model drug (e.g. Anti-viral).
3. Selection of suitable polymer.
4. Preparation of solid dispersion by suitable method.
5. Characterization of solid dispersion by FT-IR.
6. Formulation into tablet dosage form.
7. In-vitro dissolution studies.
8. Stability study.

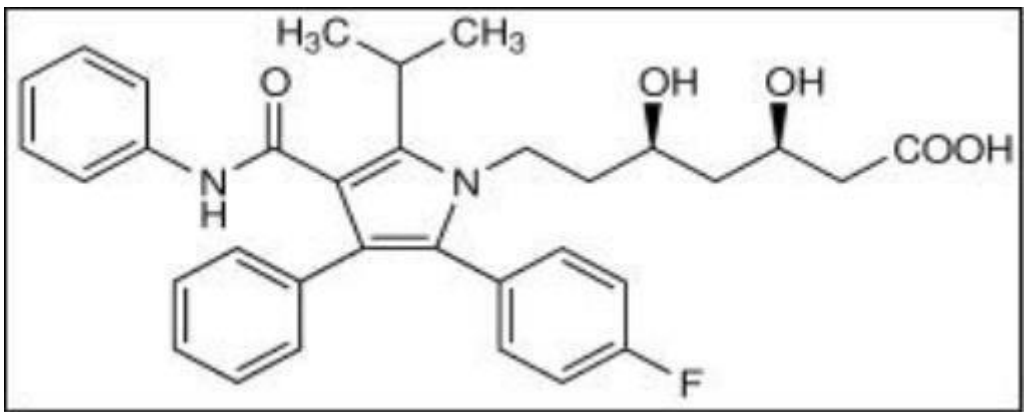
IV. DRUG & POLYMER PROFILE

Drug and Polymer Profile

4.1 Atorvastatin calcium

The atorvastatin calcium was selected for development of solid selfnanoemulsifying approaches.

Chemical structure：



IUPAC name:

Calcium (βR,δR)-2-(p-fluorophenyl)-β,δ-dihydroxy-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)pyrrole-1-eptanoicacid: (1:2) trihydrate.

Molecular formula:[C33H35FN2O5]2Ca.3H2O

Molecular weight : 1 209.4 g/mol.

Description : White to white, white amorphous powder.

Melting point : 15: 9.2- 160.7 ºC.

Freely soluble in methanol and soluble in dimethylsulphoxide (DMSO) and dimethyl formamide (DMF); insoluble in aqueous solution with pH less than 4.0. It is very slightly soluble in distilled water, Phosphate buffer (7.4) and acetonitrile; slightly soluble in ethanol. 20.4 µg/mL (pH 2.1), 1.23 mg/mL (pH 6.0).

Solubility Category: Cardiovascular agent

Sub-catogory : HMG-CoA Reductase Inhibitor Rate virtue : 98-100%

Steadiness : Stable under standard conditions.

System of Action: Atorvastatin brings down plasma cholesterol and lipoprotein levels by restraining HMG-CoA reductase and cholesterol union in the liver and by expanding the number of hepatic LDL receptors on the cell-surface to upgrade take-up and catabolism of LDL; Atorvastatin likewise decreases LDL generation and the quantity of LDL particles.

Retention: After oral organization alone, Atorvastatin is quickly retained; most extreme plasma fixations happen inside 1 to 2 hrs. Degree of ingestion increments in extent to Atorvastatin measurements. The total bioavailability of Atorvastatin (parent sedate) is around 14% and the fundamental accessibility of HMG-CoA reductase inhibitory movement is roughly 30%. The low foundational accessibility is ascribed to presystemic leeway in gastrointestinal mucosa and/or hepatic first-pass digestion. In spite of the fact that nourishment diminishes the rate and degree of medication retention by roughly 25% and 9%, individually, as evaluated by Cmax and AUC, LDL-C decrease is comparative whether Atorvastatin is given with or without nourishment. Plasma Atorvastatin focuses are lower (around 30% for Cmax and AUC) following night sedate organization contrasted and morning. In any case, LDL-C decrease is the same paying little heed to the season of day of medication organization. A blood/plasma proportion of roughly 0.25 demonstrates poor medication infiltration into red platelets. In light of perceptions in rats, Atorvastatin calcium is probably going to be discharged in human drain.

Dispersion: Mean volume of dispersion of Atorvastatin is around 381 liters. Atorvastatin is = 98% bound to plasma proteins. A blood/plasma proportion of around 0.25 shows poor medication entrance into red platelets. In view of perceptions in rats, Atorvastatin calcium is probably going to be emitted in human drain Precautions: Statins ought not be given to patients with dynamic liver ailment or unexplained tirelessly raised serum-aminotransferase fixations and ought to be ended if checked or tireless increments in serum-aminotransferase fixations happen. They ought to be abstained from amid pregnancy since there is a probability that they could meddle with fetal sterol combination; there have been a number of reports of inherent irregularities related with statins. Statins may cause myopathy and rhabdomyolysis, particularly at higher measurements, and they ought to be utilized with alert in patients in danger of rhabdomyolysis, and especially in patients taking medications that expansion plasma groupings of the statin; the statin ought to be suspended if creatine phosphokinase increments fundamentally or if myopathy is analyzed. A few statins, for example, Fluvastatin, Pravastatin, rosuvastatin, and Simvastatin, ought to be utilized with alert in patients with serious renal impedance.

Unfriendly responses: The commonest unfriendly impacts of treatment with Atorvastatin and other statins are gastrointestinal unsettling influences. Other antagonistic impacts announced incorporate cerebral pain, skin rashes, dazedness, obscured vision, a sleeping disorder, and dysgeusia. Reversible increments in serum-aminotransferase focuses may happen and liver capacity ought to be surveyed before treatment is started and then checked intermittently until multi year after the last height in measurements. Hepatitis and pancreatitis have been accounted for. Touchiness responses including hypersensitivity and angioedema have likewise happened. Myopathy, described by myalgia and muscle shortcoming and related with expanded creatine phosphokinase fixations, has been accounted for, particularly in patients taking statins simultaneously with Cyclosporine, fibric corrosive subsidiaries, or nicotinic corrosive. Once in a while, rhabdomyolysis with intense renal disappointment may create.

V. EXPERIMENTAL

Experimental Materials:

Table.3 List of Selected Excipients and Drug

Sr. No.	Name of Materials	Supplier
1	Atorvastatin calcium	Torrent Pharmaceuticals ,Ahmadabad, India
2	Maltose monohydrate	Aurochem Pharma, Mumbai, India.
4	Hydrochloric Acid	Loba Chem., Mumbai, India.
5	Potassium Chloride	Loba Chem., Mumbai, India.
6	Sodium Hydroxide	Loba Chem., Mumbai, India.
7	Microcrystelline Cellulose	Fisher Scientific, Mumbai, India.
8	Magnesium State	Fisher Scientific, Mumbai, India.
9	Collidal Silica	S.D. Fine Chem. Ltd., Mumbai, India
10	Talc	Fisher Scientific, Mumbai, India.

Instruments:

Sr.No.	Instrument Name	Model and Manufacturer
1.	Tablet Compression Machine	Cadmach, Ahmadabad, India.
2	USP Dissolution Apparatus Type II	Electrolab Limited. Ahmadabad, India.
3	UV-Visible Double Beam Spectrophotometer	Systronics, Model No. 2201, Ahmadabad, India.
4	Electronic Balance Model	Schimadzu, Japan.
5	pH Meter	Labtronics, Mumbai, India.
6	Hardness Tester	Monsanto Tester, India.
7	Friability Tester	Labtronics Roche Friabilator, India.
8	Hot Air Oven	Bio-Technics, India.
9	Disintegration Test Apparatus	Remi Pharma, Mumbai, India.
10	Ultrasononic Bath Sonicator	Bio-Techniques, India.
11	Rotatory Shaker	Remi, India.

Solubility Studies

- Phase solubility studies
- Preparation of Atorvastatin Calcium with Carriers and maltose monohydrate

1. Physical mixture

2. Solid dispersion

a) Hot melt method

b) Kneading method

Sr. No.	Physical Mixture	Drug: Polymer
1	Atorvastatin Calcium : maltose monohydrate	1:1
2	Atorvastatin Calcium : maltose monohydrate	1:2

Formulation and Evaluation of the Dosage Form Physical Evaluation of Tablet Blend

1. **Angle of Repose**

$\tan\theta = h/r$ Where,

h = height of cone

r = radius of powder cone

2. **Bulk Density**

Bulk density (g/ml) = M/Vo

Where,

M = mass of powder

Vo = apparent unstirred volume

3. Tapped Density

Tapped density (g/ml) = M/Vf

Where,

M = weight of sample powder

Vf = tapped volume

4. Compressibility

Compressibility Index = Tapped density - Bulk density

Tapped density 100

5. Hausner's ratio

Hausner ratio = Tapped density

Bulk density

VI. RESULT & DISCUSSION

1 .Melting Point Determination:

The melting point of Atorvastatin calcium was found to be159-160.7ºC which complies with the reported literature.

2. Determination of λmax :

Wavelength of maximum absorbance (λmax) for the solution of the Atorvastatin calcium prepared in pH 7.4 buffer solution was found to be 241 nm which was concordant with given literature.

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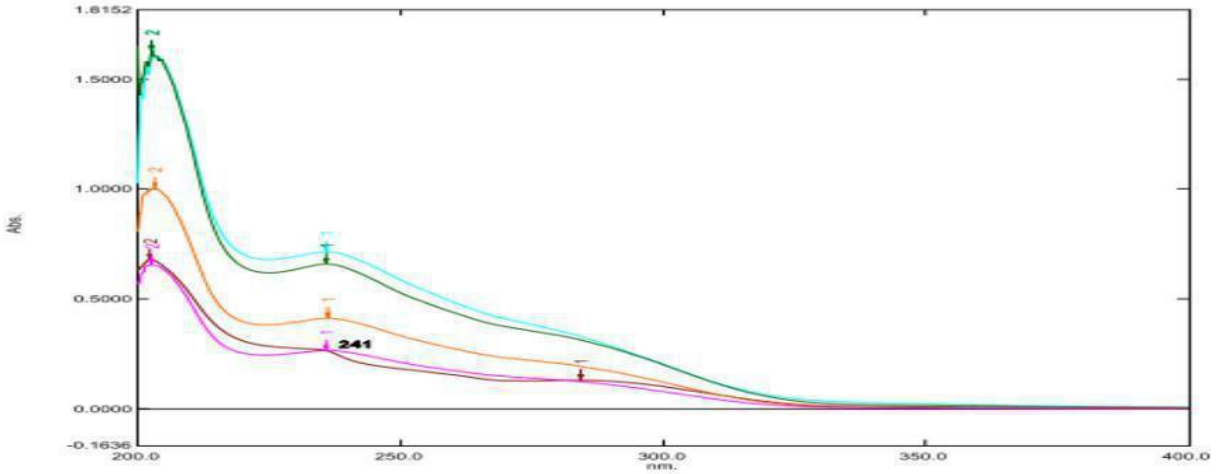

Fig.1 Spectrum of Acyclovir

Table. 4 Results of Calibration Curve

Concentration (µg/ml)	Absorbance		
	pH 1.2 Buffer	pH 7.4 Buffer	Distilled Water
2	0.215	0.048	0.194
4	0.429	0.087	0.364
6	0.632	0.125	0.533
8	0.846	0.161	0.701
10	1.047	0.201	0.883

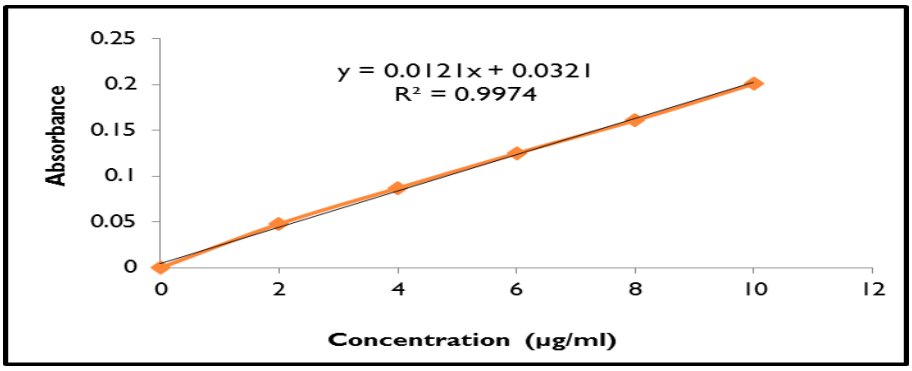

Fig.2 Calibration Curve of ATC in 0.1N HCL Buffer Solution

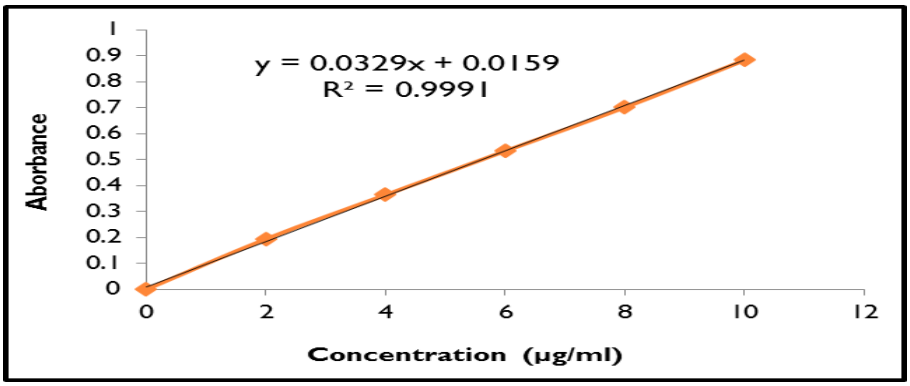

Fig.3 Calibration Curve of ATC in Distilled Water

3. Phase Solubility Studies

The phase solubility studies were performed to determine stoichiometric proportions of Atorvastatin calcium and carriers and Maltose monohydrate.

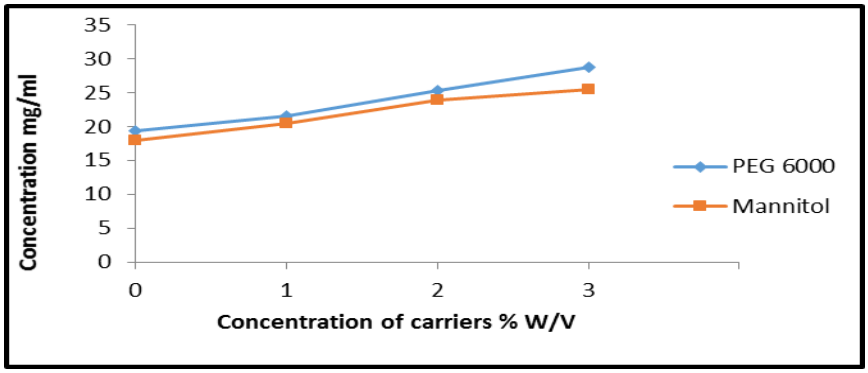

Fig.4 Results of Concentration of Carriers on Solubility of Atorvastatin calcium

Sr.no.	Concentration Of Mannitol (%w/v)	Concentration of Acyclovir in water (µg/ml)at Room Temperature
1	00	18.00±0.04
2	01	20.42±0.09
3	02	23.83±0.36
4	03	25.46±0.49

4. Analysis of Drug Content

Table.5 Results of Drug Content with MM

Methods	Ratio	Medium	
		pH 1.2 Buffer	pH 7.4 Buffer
Physical Mixture	1:1	90.20 ±0.8	90.02 ±0.5
	1:2	92.82 ±0.05	92.01 ±0.04
	1:3	91.25±0.34	93.09 ±0.25
Hot Melt Method	1:1	100.62±0.06	91.86 ±0.29
	1:2	101.57±0.65	93.52 ±0.22
	1:3	102.50±0.73	100.28±0.16
Kneading Method	1:1	98.54±0.04	98.28 ±0.75
	1:2	99.38±1.34	97.23 ±0.88
	1:3	100.41±0.76	99.36 ±2.26

Table.6 Results of Drug Content with Maltose monohydrate

Methods	Ratio	Medium	
		pH 1.2	pH 7.4 Buffer

		Buffer	
Physical Mixture	1:1	91.88 ±0.07	90.41 ±0.03
	1:2	92.18 ±0.05	91.88 ±0.06
	1:3	93.38 ±0.03	90 ±0.05
Hot Melt Method	1:1	98.94 ±0.18	99.16±1.01
	1:2	99.16 ±0.61	100 ±0.11
	1:3	100.92± 0.11	100.32 ±0.9
Kneading Method	1:1	99.54 ±1.09	98.33 ±0.02
	1:2	100.26 ±1.04	99.07 ±0.7
	1:3	99.44 ±1.17	100 ±0.4

5. Saturation Solubility Study

In order to study the saturation solubility of all solid dispersions prepared by maltose monohydrate in pH 1.2 and pH 7.4 Buffers

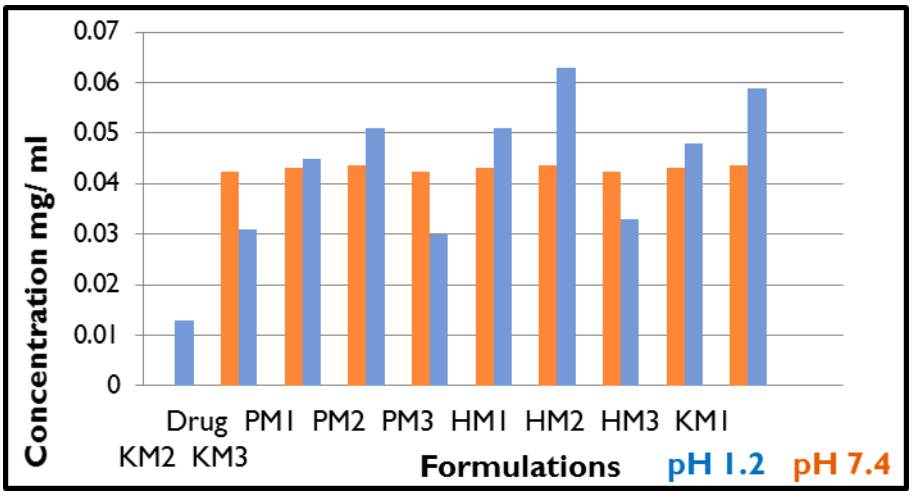

Fig.5 Results of Solubility of Atorvastatin calcium, PM and SDs with maltose monohydrate

Samples	Ratio	Solubility of Atorvastatin calcium (mg/ml)	
		pH 1.2 Buffer	pH 7.4 Buffer
Drug	-	0.013 ±0.02	0.013 ±0.02

Physical Mixture	1:1	0.031 ±0.01	0.031 ±0.01
	1:2	0.045 ±0.01	0.041 ±0.03
	1:3	0.051 ±0.02	0.045 ±0.01
Hot melt Method	1:1	0.030 ±0.06	0.051 ±0.02
	1:2	0.051 ±0.01	0.030 ±0.06
	1:3	**0.063 ±0.01**	0.044 ±0.01
Kneading Method	1:1	0.033 ±0.03	0.041 ±0.03
	1:2	0.048 ±0.04	0.029 ±0.01
	1:3	0.051 ±0.01	0.030 ±0.01

6. Characterization of Solid Dispersion System Transform Infra-Red Spectroscopy

Fourier transform Infrared spectroscopy has been used to assess the interaction between carrier and drug molecule. The FTIR spectrum of pure drug, maltose monohydrate and solid dispersion prepared by hot melt method.

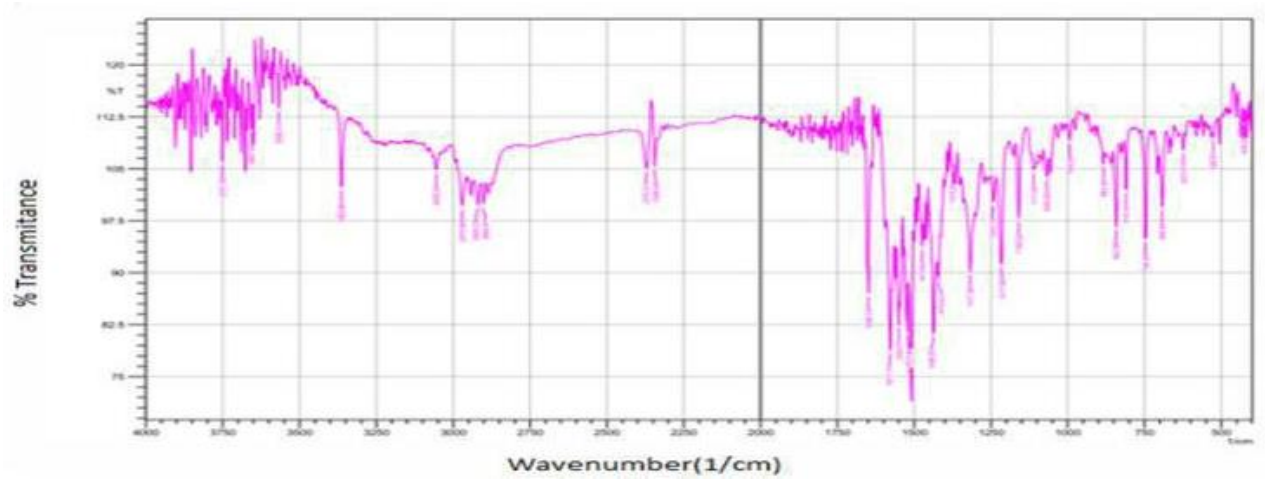

Fig.6 FT-IR Spectrum of Atorvastatin calcium

VII. CONCLUSION

Numerous Pharmaceutical medications experience the ill effects of poor watery solubility. Poor watery solubility is an exceptionally difficult issue in tranquilize detailing improvement. Along these lines, to find suitable definition ways to deal with enhance fluid solubility of ineffectively water dissolvable medications. Atorvastatin calcium is an antiviral medication. It is somewhat solvent in water and its retention is dissolution rate constrained. Along these lines to improve the dissolution rate of Atorvastatin calcium by solid dispersion with regular water powered polymers, for example, maltose monohydrate were arranged by hot Melt technique and working strategy. In the wake of contrasting the solubility and dissolution profile of different solid dispersions, it was watched that solid dispersion arranged by Hot soften strategy utilizing maltose monohydrate (1:3) appeared better dissolution profile when contrasted with other proportion.

The immersion solubility of medication was observed to be more in solid dispersion as contrasted with its unadulterated shape. The stage solubility contemplate demonstrates the presence of medication /polymer communications. Expanding the medication bearer proportion from 1:1 to 1:3 enhanced medication discharge profiles seen in for all plans if there should be an occurrence of Hot dissolve technique maltose monohydrate however in Hot liquefy strategy the medication discharge rate was higher in 1:3 proportion for the polymer. The dissolution conduct of all solid dispersion was observed to be pH subordinate. It was found for every single solid

dispersion that the dissolution diminished with expanded in pH of medium. The higher dissolution was observed to be in pH 1.2.

The tablets arranged from enhanced solid dispersion were assessed for precompression and post pressure parameters and were observed to be palatable. The definition demonstrated outcomes for weight variety 1296.5 ± 0.45, friability 0.48 ± 0.50 %, thickness 4.84 ± 0.06 mm, content consistency 99.35 ± 0 .67 and breaking down time 12± 0.40 min.

The rate medicate arrival of definition in pH 1.2 and pH 7.4 was found to be 94.11% of every 40 min and in Mannitol 82.23% out of 60 min individually. From the above outcomes, it was presumed that the enhanced medication dissolution could be accomplished by detailing Atorvastatin calciumas a solid dispersion with the polymers, for example, maltose monohydrate. . In this way the examination demonstrated that the reasonableness of maltose monohydrate as transporter for the readiness of Atorvastatin calcium solid dispersion and dissolution rate of Atorvastatin calcium can be upgraded to an extraordinary degree by utilizing modernly hot soften strategy on account of synergistic impact of solubilization utilized for dissolvable diminishes crystallinity prompting change in dissolution rate. Additionally, it was watched that all plans demonstrated pH subordinate dissolution rate i.e. higher dissolution rate in pH 1.2 Buffer when contrasted with other.

VIII. FUTURE WORK

In proposed work delivery predictability is calculated by using three metrics as-number of encounters between nodes, time span between their meetings and transitive property of delivery predictability. It will be interesting to evaluate delivery predictability by using different metrics like context information and history of nodes.

REFERENCES

[1] **Sharma DK, Joshi SB. Solubility enhancement strategies for poorly watersoluble drugs in solid dispersions: A review. Asian J Pharm 2007; 1(1): 9-19.**

[2] **James S, James CB. Encyclopedia of pharm techn. New York: Informa Health care 2000.**

[3] **Hussain MD, Kurniasih D, Stith C, Habib MJ. Solid dispersions of Mifepristone :Preparation and in-vitro evaluation. School of Pharmacy, Animal Science, University of yoming, School of Pharmacy, Howard University.**

[4] **Tayyab Ansari M and Sunderland VB. Solid dispersions of Dihydroartemisinin in Polyvinylpyrrolidone. Arch Pharm Res 2008; 31 (3):390-398.**

[5] **Chaulang G, Patil K, Ghodke D, Khan S and Yeole P. Preparation and characterization of solid dispersion tablet of Furosemide with Crospovidone. Res J Pharm and Tech 2008;1(4).**

[6] **Tantishaiyakul V, Kaewnopparat N. Properties of solid dispersions of Piroxicam in Polyvinylpyrrolidone. Intern J of Pharm1999; 181:143–151. Bhise S et al.**

[7] **Enhanced solubility and dissolution of Telmisartan by solid dispersion techniques. Intern J of Pharma Res and Sci 2011; 2(98): 485-492.**

[8] **Shavi GV et al. Enhanced dissolution and bioavaibility of Gliclazide using solid dispersion techniques. Intern J of Drug Del 2010; 2: 49-57.**

[9] **Patel T et al. Enhancement of dissolution of Finofibrate by solid dispersion technique. Intern J Res Sci 2010; 1(2):127-132.**

[10] **Islam MS. Improvement of dissolution of Ibuprofen and Finofibrate by Poloxamer based solid dispersion. Bangladesh Pharm J 2010; 13(1): 54-59.**

[11] **Rahamat Ulla M, Gangadharappa HV, Solubility and dissolution improvement of Rofecoxib using solid dispesion technique.**

[12] **Ansari MT, Sundarland VB. Solid dispersion of Dihydroartemisinin in Flunarizine and Polyvinylpyrrolidone. Farmaco 2002; 57: 723-727.**

[13] **Saharan VA, Kukkar V, Kataria M, Gera M, Choudhury PK. Dissolution enhancement of drugs. Part I: Technologies and effect of carriers. Intern J of Health Res 2009; 2(2):107-124.**

[14] Vasconcelos T, Sarmento B, Costa P. Solid dispersion as a strategy to improve bioavailability of poor water soluble drugs. Drug Discovery Today 2007;12 (23/24):1068-75.

[15] Ducam QM.,Craig. The mechanisms of drug release from solid dispersions in water-soluble polymers. Intern J Pharm 2001; 231:131-44.

[16] James S, James CB. Encyclopedia of pharmaceutical technology. New York: Informa health care; 2000.

[17] Ducam QM, Craig. The mechanisms of drug release from solid dispersions in water-soluble polymers. Intern J Pharm 2001; 231:131-44.

[18] Lewis S, Dhirendra K, Udupa N, Atin K. Solid dispersions: A Review Pakistan J Pharm Sci 2009; 22(2): 234-46.

[19] Ducam QM., Craig. The mechanisms of drug release from solid dispersions in water-soluble polymers. Intern J Pharm 2001; 231: 131-44.

[20] Sharma DK, Joshi SB. Solubility enhancement strategies for poorly water-soluble drugs in solid dispersions: A review. Asian J Pharm 2007; 1(1):9-19.

[21] James S, James CB. Encyclopedia of pharmaceutical technology. New York: Informa health care; 2000.

[22] Saharan VA, Kukkar V, Kataria M, Gera M, Choudhury PK. Dissolution enhancement of drugs. Part I: Technologies and effect of carriers. Intern J of Health Res 2009; 2(2):107-124.

[23] Chandra D et al.Enhanced dissolution and solubility of Artesunate using slid dispersion techniques.Intern J of Medicine and Pharma Research 2014; 2(1): 451-461.

[24] Shinde SS et al.Prepration and characterization of Atrovastatine by solid dispersion techniques.Intern J of Pharma and Res Sci 2014; 5(3): 1014-1044.