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DESIGN, DEVELOPMENT AND EVALUATION OF SUBLINGUAL TABLET OF CILNIDIPINE (ANTIHYPERTENSIVE) USING NATURAL SUPER DISINTEGRANT

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ABSTRACT

Objective: In the present reported project study, the effect of Natural superdisintegrant was compared with synthetic super disintegrants and conventional super disintegrants in the Sublingual tablet formulation of Clinidipine. Cilnidipine is the novel dihydropyridine calcium antagonist and calcium antagonistic activity of clinidipine is long lasting than those of Nifedipine and Nicardipine. Cilnidipine has been used for the treatment of any hypertension and hypertensive-associated vascular disorders. Cilnidipine shows a very low solubility (BCS Class-II drug Low solubility high permeability) and compliance to the medication is always very poor The dissolution rate is directly proportional to solubility of drug. **Methods:** In the present work, 9 formulations of Sublingual tablets of Clinidipine were prepared by using natural superdiintegrants was evaluated and compiles with the official standards, parameters and specifications. Various formulations were prepared using three types of different superdisintegrant namely- Banana Powder, sodium starch glycolate, cross carmelose sodium with three concentrations (2%, 4%, 6%) by direct compression method. **Result:** The blend was evaluated for pre-compression parameters like Angle of repose, bulk density, tapped density, and then tablet evaluated post-compression parameters like thickness, drug content, hardness, weight variation, wetting time, friability, disintegration time, dissolution time, drug release study. Formulation SLT8 showed the lowest disintegration time and in-vitro

dissolution studies recorded that formulation SLT showed Better drug release at the end of 3 minutes. **Conclusion:** The best formulations were also found to be stable and optimized formulations were subjected to the stability studies as per ICH guideline and standards.

KEYWORDS: Sublingual tablet, Clinidipine, Co-proceed, sodium starch glycolate, Natural, Banana Powder direct compression, dissolution time.

INTRODUCTION

The tablet is most widely used dosage for because of its convenience in term of self-administration, compactness, accurate drug dose and ease in manufacturing. Over this one drawback of conventional tablet is difficulty in swallowing by pediatric and geriatric patients.[1,2]

To beat these issues the scientists have developed novel drug delivery system that known as Sublingual tablet. The Sublingual defined as the tablets that dissolve in few seconds in the mouth when they come with contact saline without requirement of additional water. The advantage of FDT is onset of action, higher patient acceptance, and increased bioavailability.[3,4]

Cilnidipine is a novel and unique dihydropyridine calcium channel blocker that possesses a slow-onset, long-lasting vasodilating effect. It is a 4th generation dihydropyridine (DHP) type of calcium channel antagonist. Unlike other calcium channel antagonists, cilnidipine has dual action blocks the influx of Ca2+ ions into both vascular smooth muscle at the level of L-type Ca2+ channels and neuronal cells at the level of N-type Ca2+ channels.

Bioavailability of Clinidipine is about 80% to 90% and its half-life is 4-4.5 h. The drug is distributed throughout the body and 90% of drug binds to plasma proteins. It undergoes rapid first-pass metabolism in the liver (approximately 95% of a dose). This leads to lower bioavailability of Clinidipine. In order to overcome such extensive first-pass metabolism effect, so the drug is selected for Sublingual tablet.[5,6,7,8,9]

MATERIAL AND METHOD

MATERIAL

Cilnidipine was a gift sample from Emcure Pharmaceuticals Pvt. Ltd. Pune, Magnesium stearate used were procured from Reckon animal health care, Jaipur, Lactose used was procured from Rescue laboratories, Jaipur, Banana Powder was gifted by Krishna Herbals,

Delhi, Aspartame used was procured from Sweetener India, Delhi, and other reagents and chemicals used were of analytical grade.

METHOD

Sublingual tablets of Clinidipine were prepared by direct compression method. Pure API drug and excipients were passed through # 60 No. mesh. Required amount of drug and excipients were taken for every formulation according Table No. 1.

The powdered pure drug, Mannitol and Lactose were mixed uniformly with continuous triturating using mortar and pestle. Then required quantity of super disintegrates and aspartame taken for each formulation and mixed, finally magnesium stearate and talc powder were added and mixed well.[10,11,12]

The mixed blend of drug and excipients were compressed by using 7 station tablet punching machine. (Shakti pharmaceuticals**)** 4 Mm punch. A Batch of 100 tablets of each formulation were prepared for all the designed formulation. Before the tablet preparation punch the mixture blend of all designed formulations were subjected to compatibility studies (IR) and pre-compression parameters like- Angle of repose, Bulk density, Tapped density, compressibility index, Hauser's ratio.[13,14,15]

PRE-FORMULATION STUDIES

Angle of Repose (θ)

Angle of repose is the maximum possible angle between the surface of the pile of the powder and the horizontal plane of the powder. When more quantity powder is added to the pile, it slides down, until the mutual friction of the particles producing a surface angle θ, is equilibrium with the gravitational force.[15,16,17]

The angle of repose was determined by the funnel method suggested by the scientist Newman. Angle of repose is determined by the following formula

$$\text{Tan } \theta = h/r$$

$$\theta = \text{Tan}^{-1}\, h/r$$

Where θ = Angle of repose, r = Radius of the cone, h = height of the cone

Bulk Density

Density is weight mass per unit volume. Bulk density is defined as the mass of the powder is divided by the bulk volume of powder and is expressed as gm/cm^3. The bulk density of a

powder primarily depends on its, particle shape, particle size, distribution and the tendency of particles to adhere together. There are two types of bulk density.[18,19,20,21]

Low bulk density

The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density.

High bulk density

Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density.

Tapped Density (DT)

It was the ratio of total mass of the powder to tapped volume of the powder. Volume was reported by tapping the powder for 500 times and the tapped volume was observed, if the difference between these two volumes was less than 2%. If it more than 2%, then tapping was continued for 750 times and tapped volume was noted. Tapping was continued until the difference between volumes was less than 2% in bulk density apparatus. It was expressed in g/ml and was given as following,

$$DT = M/Vt$$

Where, M is the mass of powder

Vt is the tapped volume of the powder.[22-24]

Carr's index (or) % compressibility

Carr's index indicates powder flow properties. It is expressed by percentage and is given by:

$$I = DT - Db/DT \times 100$$

Where, DT denotes the tapped density of the powder

And Db is the bulk density of the powder.[25,26,27,28]

Hausner ratio

Hausner ratio is an indirect index of ease of powder flow properties. It is calculated by the following formula:

$$\text{Hausner ratio} = Dt/Db$$

Where, Dt show the tapped density., Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25)

EVALUATATION OF TABLET

All prepared tablets of Clinidipine were evaluated for the following parameters as per IP guideline and standards for all the calculations are represented in the table No.3.

WEIGHT VARIATION

Twenty tablets of Clinidipine formulation were selected randomly from each of the formulation and weighted individually using Windsar Digital Balance for their weight variation data. The average weight of the tablets as well as percentage deviation was calculated.[29,30,31]

HARDNESS

Hardness of the Clinidipine tablets were measured with Monsanto tablet hardness tester for evaluation the hardness of the tablets.

THICKNESS

The thickness of the tablet was measured in mm by the Vernier Calipers for all the designed formulation batches.

FRIABILITY

The Friability of the Clinidipine tablet by a sample of twenty tablets was measured using USP type Roche Friabilator. The tablets were dusted reweighed and percentage weight-loss was calculated.

$$\%\text{Friability} = \text{Initial Weight} - \text{Final Weight} * 100 / \text{Initial Weight}$$

Water absorption ratio

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in small Petri-plate (ID = 6.5 cm) containing 10 ml of water. A tablet was placed on the paper and time for complete wetting of the tablet was measured in seconds. Three trials for each batch were performed and the standard deviation was also determined. The wetted tablet was weighed and water absorption ratio R, was determined by following equation

$$\mathbf{R = \{(Wa - Wb) / Wa\} \times 100}$$

Where, Wa and W_b were weights of the tablets after and before study.[33,34,35]

Wetting Time

A piece of tissue paper (12cmX10.75cm) folded twice was placed in a small Petri dish (ID = 9 cm) containing 5ml pH 6.8 phosphate buffer, A tablet was placed on the paper and the time

taken for complete wetting was observed. Three tablets from each formulation were randomly selected and the average wetting time was noted.

DISINTEGRATION STUDY

Disintegration time study was carried out by selecting 6 tablets of Clinidipine and performed disintegration test (Lab India) using 900 ml distilled water at temperature ($37^0C \pm 2^0C$).[36,37,38]

DISSOLUTION STUDY

The In-vitro for the dissolution study was carried out in the USP (United state pharmacopeia) dissolution test apparatus type II known as Paddle dissolution apparatus, used phosphate buffer as dissolution medium as 900 ml containing PH 6.8 was taken in vessel and the temperature maintained at 37 ± 0.5^0C. The speed of the paddle was set at RPM 50, then 5 ml dissolution medium was withdrawn and the same amount (5ml) of fresh medium was replenished to the dissolution medium. The calculations of the Concentration were calculated by absorbance base. The release of the drug was performed in replicates of three.

Table No. 1: Formulation of Sublingual tablet of Clinidipine.

Ingredients(mg)	SLT1	SLT2	SLT3	SLT4	SLT5	SLT6	SLT7	SLT8	SLT9
Clinidipine	80	80	80	80	80	80	80	80	80
Crosspovidone	4	8	12	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	4	8	12	-	-	-
Banana Powder	-	-	-	-	-	-	4	8	12
Aspartame	2	2	2	2	2	2	2	2	2
Flavour	2	2	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Mannitol	58	58	58	58	58	58	58	58	58
Lactose	50	46	42	50	46	42	50	46	42
TOTAL	200	200	200	200	200	200	200	200	200

Table No. 2: Pre-compression parameters of Clinidipine Sublingual tablet.

Parameters Formulation code	Bulk density (g/cm3)*	Tapped density (g/cm3)*	% Compressibility index	Hausner's ratio	Angle of repose
SLT1	0.415±0.07	0.532±0.05	21.99	1.28	29.02
SLT2	0.430±0.05	0.522±0.03	16.35	1.19	28.25
SLT3	0.432±0.02	0.540±0.07	17.62	1.21	30.12
SLT4	0.430±0.03	0.522±0.04	17.62	1.21	31.06
SLT5	0.435±0.06	0.520±0.06	16.35	1.19	32.08
SLT6	0.415±0.09	0.532±0.09	21.99	1.28	28.78

SLT7	0.415±0.07	0.532±0.04	21.99	1.28	32.08
SLT8	0.435±0.04	0.535±0.08	17.14	1.20	28.45
SLT9	0.432±0.05	0.540±0.06	20.00	1.25	29.67

Table No. 3: Post-Compression parameters of Clinidipine Sublingual tablet.

Formulation	Parameters						
	Diameter (mm)	Thickness (mm)	Weight (mg)	Hardness (Kg/cm2)	Friability (%)	Disintegration Time (Sec)	Swelling Time (Sec)
SLT1	6.0	2.5	200.15±3.85	3.44	0.49	52±1.42	12±03
SLT2	6.0	2.5	199.75±3.32	3.32	0.47	54±1.36	14±04
SLT3	6.0	2.5	200.8±3.47	3.39	0.43	49±1.21	17±02
SLT4	6.0	2.5	201.20±3.64	3.60	0.47	48±2.15	11±05
SLT5	6.0	2.5	200.94±2.79	3.65	0.44	43±2.13	16±04
SLT6	6.0	2.5	201.55±2.18	3.81	0.44	39±1.81	15±02
SLT7	6.0	2.5	200.35±3.70	3.42	0.48	55±2.19	18±03
SLT8	6.0	2.5	200.30±3.54	3.75	0.46	44±2.77	13±06
SLT9	6.0	2.5	203.45±3.87	3.62	0.45	38±1.35	11±06

Table No. 4: Drug Content in the Sublingual Tablet of Clinidipine.

Formulation	Parameters	
	Drug Content (mg per Tablet)	% Drug Content
SLT1	19.498±0.025	97.49
SLT2	19.293±0.049	101.46
SLT3	20.480±0.142	102.01
SLT4	19.412±0.025	97.06
SLT5	19.566±0.041	98.93
SLT6	19.549±0.018	100.74
SLT7	20.532±0.023	97.66
SLT8	19.498±0.011	102.66
SLT9	20.312±0.050	101.26

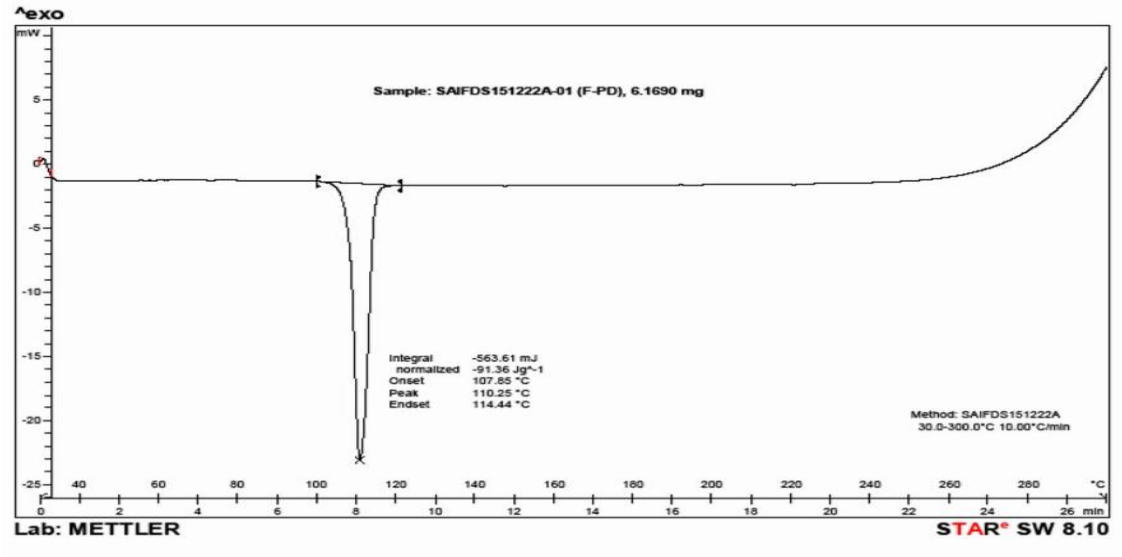

Figure.2: DSC Thermogram of Clinidipine.

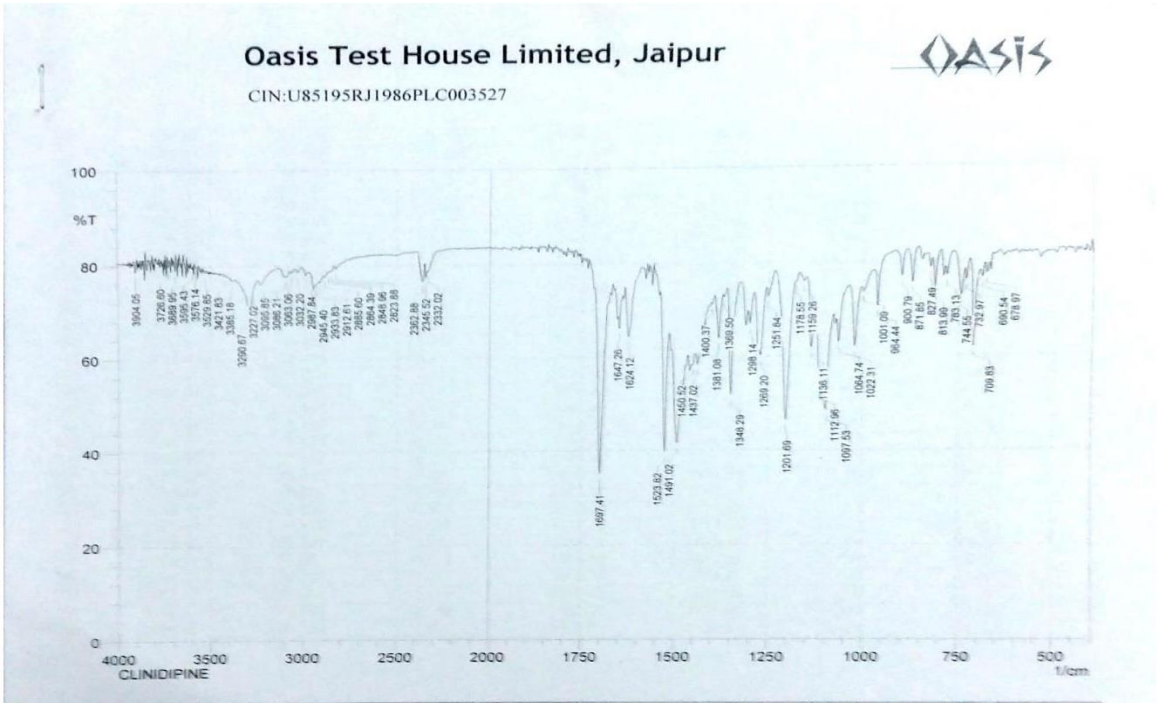

Figure.3: IR Spectra of Clinidipine.

RESULTS AND DISCUSSION

Bulk Density and Tapped Density of the Blend were found as 0.415 to 0.435 and 0.520 to 0.540 respectively. Carr's index of the prepared blend fall in the range of 11.11 to 15.38% and this is also supported by Hausner's factor values which were in the range of 1.120 to 1.180. Hence the prepared blends posses good flow property and can be used for manufacturing of the tablet. The values of angle of repose were found in the range of 26.03 to 28.52. The average weight of the sublingual tablet was 199.75 to 200.92mg. Hardness of prepared tablet was between 3.32 to 3.81 kg/cm^2. The percent friability of formulations was found to be 0.43 to 0.49 (less than 1.0%) and thus hardness and friability of all formulation are found within the acceptable limit.

The disintegration time is very important and it is desired to be less than 1 minute. The quick disintegration may assist quick swallowing and drug absorption in buccal cavity, thus greater bioavailability of the drug. Disintegration time of prepared sublingual tablet was found in the range of 38 to 58 seconds. Swelling time is the indicator for the ease of disintegration of the tablet in the buccal cavity. It was observed that swelling time of tablet was in the range of 11 to 18 seconds. It was found that the nature of superdisintegrants present affected the swelling of the tablets. In Vitro dissolution study: In vitro dissolution study was performed by using

Methanolic Sorenson's buffer pH 6.8 as dissolution medium using dissolution test apparatus LAB INDIA DS 8000 at a paddle speed of 50 rpm. At the end of 6 minutes the cumulative percentage drug release from various fast dissolving tablets was found to be 97.49%, 101.46%,, 97.06%, 98.93%, 100.74%, 97.66%, 102.66% 98.49% and 101.26% from SLT1, SLT2, SLT3, SLT4, SLT5, SLT6,SLT7, SLT8 and SLT9 respectively. This clearly indicates that when superdisintegrants are used in combination than they provides better release than alone.

CONCLUSION

It can be concluded from the whole study that Sublingual tablets of Clinidipine drug. Natural superdisintegrant can be used as pharmaceutical excipients for oral drug delivery. So natural superdisintegrant like Banana Powder exhibited faster drug dissolution which leads to improve bioavailability, effective therapy (Therapeutic ratio), improve patient compliance, and satisfies all the standards as Sublingual tablet. It was concluded formulation SLT8 maximum percentage drug release was found 102.66, with Natural Banana Power 4%.

From the study, it was concluded that Banana powder superdisintegrant showed better disintegrating property over the synthetic super disintegrate like, SSG(Sodium starch glycolate) CP (Crospovidone).

REFERENCES

1. Sharma ashok kumar, et al., Formulation and evaluation fast dissolving tablet of tizanidine HCl using fenugreek seed mucilage by direct compression method, IJPSR, june, 2017; 1(2): 38-42.
2. Vikas Sharma, Vandana Arora, Chanda Ray Use of Natural superdisintegrant In Mouth Dissolving Tablet- an Emerging Trend International Bulletin of Drug Research., 2016; 1(2): 46-54.
3. M. M. Patel and D. M. Patel Research Paper Fast Dissolving Valdecoxib Tablets Containing Solid Dispersion of Valdecoxib [Downloaded Free From Http://Www.Ijpsonline.Com on Wednesday, April 20, 2016.
4. C. Mallikarjuna Setty, D. V. K. Prasad, V. R.M. Gupta and B. Sa1 Research Paper Development Of Fast Dispersible Aceclofenac Tablets: Effect Of Functionality Of Superdisintegrants, April 20, 2016.
5. D.Srinivasarao, T.Venkateswarlu And G. Rama Krishna Research Article On Development And Validation Of Hplc Method Of Dissolution Test For Metoprolol

Succinate And Cilnidipine International Journal Of Pharmaceutical, Chemical And Biological Sciences Ijpcbs, 2015; 5(4): 971-981. Srinivasa Rao Et Al. Issn: 2249-9504

6. L/N-Type Calcium Channel Blocker Cilnidipine Added To Renin-Angiotensin Inhibition Improves Ambulatory Blood Pressure Profile And Suppresses Cardiac Hypertrophy In Hypertension With Chronic Kidney Disease International Journal Of Molecular Sciences 2015 Issn 1422-0067 Www.Mdpi.Com/Journal/Ijms
7. Mr. Vallabhbhai Pansuriya, Dr. Anil Bhandari Formulation And Optimization Of Press Coated Pulsatile Tablet Of Cilnidipine For Chronopharmaceutical Approach For Treatment Of Hypertension Getz Pharma Research Pvt. Ltd, Mumbai, Maharashtra Iijpr International Journal Of Pharmacy And Pharmaceutical Research, 2015.
8. Suparna Sacchit Bakhle And Jasmine Gev Avari Development And Characterization of Solid Self-Emulsifying Drug Delivery System Of Cilnidipine Chem. Pharm. Bull, 2015; 63: 408–417 Regular Article 63, 61.
9. Mohit Mangal, Sunil Thakral, Manish Goswami, Pankaj GhaiIssn: 2249-0337 Review Article Superdisintegrants: An Updated Review International Journal Of Pharmacy And Pharmaceutical Science Research 2015 Available Online At Http://Www.Urpjournals.Com
10. A.Bharathi, Sd. Khaleel Basha. K.N.V.Deepthi And M.Ch.Phanin Formulation And Evaluation Of Telmisartan Orodispersible Tablets By Using Banana Powder Bharathi Et.Al Indian Journal Of Research In Pharmacy And Biotechnology Issn: 2321-5674.
11. Mohammad Ali Shahtalebia, Majid Tabbakhiana, Navid Sarbolookzadeh Harandic Formulation And Evaluation of Orally Disintegrating Tablets Of Captopril Using Natural Super Disintegrants Isfahan University Of Medical Science, Isfahan, Iran. Journal Of Reports In Pharmaceutical Sciences 2014
12. Yadav S. K., Pant L. M, Paudel G., Poudel N., Shrestha R. Kathmandu University Dhulikhel, Kavre, Nepal. Research Article Evaluation Of Crude Banana Powder As Formulation Additives And Comparison Of Its Mucoadhesive Property With Carbapol 934p International Journal Of Pharmaceutical Research And Bio-Science Coden: Ijprnk Impact Factor: 1.862 Issn: 2277-8713Sk Yadav, Ijprbs, 2014; 3(2): 172-183. Ijprbs.
13. Jieon Lee, Howard Lee, Kyungho Jang Kyoung Soo Lim Dongseong ShinKyung-SangYu Evaluation of the Pharmacokinetic And Pharmacodynamic Drug Interactions Between Cilnidipine And Valsartan, In Healthy Volunteers Drug Design, Development And Therapy Dovepress Original Research, 2014.
14. Sharma ashok kumar et al Formulation, Development and In-vitro Evaluation of Fast

Dissolving Tablet of Aceclofenac using co-processed Superdisintegrant by Direct Compression Method Int. J. Pharm. Sci. Rev. Res., January – February, 2019; 54(2), 12: 67-72

15. Sharma ashok kumar et al., Formulation and evaluation fast dissolving tablet of Domperidone using fenugreek seed mucilage by direct compression method, WJPPS 10.20959/wjpps20177-9580.
16. Nareda Maniratna, Sharma ashok kumar et al., Design and formulation of fast dissolving tablet of Lornoxicam using Banana powder as natural superdisintegrant by direct compression method, WJPPS 10.20959/wjpps20177-9579.
17. C. Mallikarjuna Setty, D. V. K. Prasad, V. R.M. Gupta And B. Sa1 Research Paper Development of Fast Dispersible Aceclofenac Tablets: Effect Of Functionality Of Superdisintegrants [Downloaded Free From Http://Www.Ijpsonline.Com On Wednesday, April 20, 2016, Ip: 117.211.20.165
18. Sharma Vikas, Arora Vandana, Ray Chanda Use of Natural superdisintegrant In Mouth Dissolving Tablet- an Emerging Trend International Bulletin of Drug Research., 2016.
19. Hamilton, Richart. Tarascon Pocket Pharmacopoeia 2015 Deluxe Lab-Coat Edition. Jones & Bartlett Learning, 2015; 3.
20. D.Srinivasarao, T.Venkateswarlu And G. Rama Krishna Research Article On Development And Validation Of Hplc Method Of Dissolution Test For Metoprolol Succinate And Cilnidipine International Journal Of Pharmaceutical, Chemical And Biological Sciences Ijpcbs, 2015; 5(4): 971-981 Srinivasa Rao Et Al. Issn: 2249-9504.
21. J. Hamsanandini, S. Parthiban1, A. Vikneswari, G. P. Sentil Kumar, T. Tamiz Mani Formulation and Evaluation Of Orodispersible Liquisolid Compacts Of Meloxicam Using Banana Powder As A Natural Superdisintegrants. Asian Journal of Research In Biological And Pharmaceutical Sciences, 2015; 25-38. Research Article Issn: 2349 – 4492.
22. Anisree. G. S, Anu. V, Rauof. P, Megha.V, Jouhara. O. P, Abeera. C. H.; Design and Evaluation of Mouth Dissolving Tablet of Levocetrizine Hydrochloride. Sch. Acad. J. Pharm., 2015; 3(1): 45-49.
23. Mr. Vallabh bhai Pansuriya, Dr. Anil Bhandari Formulation And Optimization Of Press Coated Pulsatile Tablet Of Cilnidipine For Chronopharmaceutical Approach For Treatment Of Hypertension Getz Pharma Research Pvt. Ltd, Mumbai, Maharashtra IIJPR International Journal Of Pharmacy And Pharmaceutical Research, 2015.
24. Bakhle Suparna Sacchit and Avari Jasmine Gev Development and Characterization of Solid Self-Emulsifying Drug Delivery System Of Cilnidipine Chem. Pharm. Bull, 2015;

63, 408–417 Regular Article, 63: 61.

25. Pentewar R.S., Somwanshi S., Thonte S.S, Talde S, Singh Anoop.:Formulation and evaluation of fast dissolving tablets of poorly soluble drug loratidine using solid dispersion and natural superdisintegrants. Indo American Journal of Pharm Research, 2014; 4(10): 4023-4035.
26. Kagalkar Amrita A., Nanjwade Basavaraj K.,Bagli R. S.: Development and Evaluation of Herbal Fast Dissolving Tablets of Tectona grandis Linn. International Journal of Pharma Research & Review, 2014; 3(1): 6-14.
27. Nagar Praveen Kumar, Parvez Nayyar, Sharma Pramod Kumar.: Formulation and evaluation of piroxicam fast dissolving tablets using different natural superdisintegrants. International journal of Pharmacy and Pharmaceutical sciences, 2014; 4(4): 55-59.
28. Ujjwal Nautiyal, Satinderjeet Singh, Ramandeep Singh, Gopal, Satinder Kakar.: Fast Dissolving Tablets as A Novel Boon: A Review. Journal of Pharmaceutical, Chemical and Biological Sciences, 2014; 2(1): 05-26.
29. Renati Damodar, Babji Movva, Vinay CV.: Role of Novel Hole Technology in Fast Dissolving Tablets. J Mol Pharm Org Process Res., 2014; 2(1): 1-5.
30. Md Tausif Alam, Nayyar Parvez, and Pramod Kumar Sharma.: FDA-Approved Natural Polymers for Fast Dissolving Tablets. Hindawi Publishing Corporation Journal of Pharmaceutics, 2014; 1-6.
31. Gupta Dilip Kumar, Bajpai Meenakshi, Chatterjee D.P.: Fast mouth dissolving disintegrating tablet and patient counselling points for fddts - A REVIEW. International Journal of Research and Development in Pharmacy and Life Sciences, 2014; 3(3): 949-958.
32. Isheen s. Shah, Hiral Shah.: A review on fast dissolving tablet. International journal of pharmaceutical research and bio-science, 2014; 3(2): 598-607.
33. Sanket Kumar, Shiv Kr. Garg, Ajay Anseri, Pradeep Luhani: Fast dissolving tablets (fdts): recent trends and new market opportunities. Indo American Journal of Pharmaceutical Research, 2014; 4(07): 3265-3276.
34. B. Sujatha, G. R. K. Mohan, M. Krishna Veni, P. Yanadaiah, B. Suman Kumar.: Effect of superdisintegrants on release of domperidone from fast Dissolving tablets. Journal of Global Trends in Pharmaceutical Sciences, 2014; 5(3): 1973–1978.
35. Subbaiah B.V, Krishnamoorthy B, Muthukumaran M.: Formulation and Evaluation of Trihexyphenidyl HCl Fast Dissolving Tablets. Int J Adv Pharm Gen Res., 2014; 2(2): 1-8.

36. Pentewar R.S., Somwanshi S., Thonte S.S, Talde S, Singh Anoop.: Formulation and evaluation of fast dissolving tablets of poorly soluble drug loratidine using solid dispersion and natural superdisintegrants. Indo American Journal of Pharm Research, 2014; 4(10): 4023-4035.
37. Lakshmi A. Geetha, Patel Ravi, Kumar Divya S.: Formulation and evaluation of fast dissolving tablets of antiemetic drug metoclopramide. World journal of pharmacy and pharmaceutical sciences, 2014; 3(8): 2080-2090.
38. Kulkarni A. S., Majumdar S. H., Aloorkar N. H., Karande K. M., Kodalkar Dada D.: Study of cross-linked sodium rboxymethylcellulose (nacmc) as an alternative superdisintegrant in fast dissolving formulation. World Journal of Pharmaceutical Research, 2014; (3)7: 396-409.
39. Gupta M.M., Gupta N. Chauhan B.S., Pandey S.: Fast Disintegrating Combination tablets of taste masked Levocetrizine dihydrochloride and Monteleukast Sodium: Formulation design Development and Characterization. Hindawi Journal of Pharmaceutics, 2014; 2(1): 1-15.
40. Pranavi P., Md. Gulsan, Gupta M.E., Rao R.N.: Formulation and evaluation of immediate release Irbesartan pellets and tablets. Indo American J. of Pharm. Res., 2014; 3: 1617-1624.
41. Subbaiah B.V, Krishnamoorthy B, Muthukumaran M.: Formulation and Evaluation of Trihexyphenidyl HCl Fast Dissolving Tablets. Int J Adv Pharm Gen Res., 2014; 2(2): 1-8.
42. Soni Amrita et al., Formulation development and evaluation of fast dissolving tablet of Ramipril, Int J Pharm Pharm Sci., 7(8): 127-131.
43. Jain C.P. and Naruka P.S., Formulation and evaluation of fast dissolving tablet of Valsartan, International Journal of Pharmacy and Pharmaceutical Sciences, July-Sep. 2009; 1: 1.
44. Patel B. et. *al*., Development and invitro evaluation of fast dissolving tablets of glipizide, International Journal of Pharmacy and Pharmaceutical Sciences, Dec. 2009; 1: 1.
45. Abdelbary G, Prinderre P, Couani C, Taochim J, Reynier JP, Riccerelle P. The preparation of orally disintegrating tablets using a hydrophilic waxy binder. Int J Pharm., 2004; 278(2): 423-33.
46. Jogala S, Ankathi L, Jarupula R.Glimepiride fast disintegrating tablets: Formulation, evaluation and in-vivo disintegration and dynamic studies. Int J Pharm, 2016; 8(5): 271-78.

47. Kumar S, Garg S. Fast dissolving tablets (FDTs): Current status, new market opportunities, recent advance in manufacturing technologies and future prospects. Int J Pharm., 2014; 6(7): 22-35.