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Research Article

DEVLOPMENT AND EVALUTION OF MOUTH DISSOLVING TABLET OF AMLODIPINE BESYLATE BY USING VARIOUS SUPERDISINTIGRANT

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Abstract

The drug Amlodipine Besylate is used commonly for the treatment angina pectoris, commonly known as angina, is chest pain due to ischemia of the heart muscle, generally due to obstruction or spasm of the coronary arteries (the heart's blood vessels). Dosing to elderly patients is improved by mouth dissolving tablets it also provides convenience to whom that have trouble in swallowing tablets.

The objective of the present study was to prepare the mouth dissolving tablet of Amlodipine using different superdisintegrants by sublimation method.

Different concentrations (2%, 4% and 6%) of superdisintegrants such as Ac-Di-Sol, Croscarmillos Sodium, Crospovidone were used respectively. Camphor was used as an sublimating agent. Tablets are prepared by direct compression and mannitol is used as bulking agent. The compressed tablets are dried for 5 hours to allow sublimation of camphor to increase the porosity of the fast dissolving tablets to improve the dissolution.

The tablets were evaluated for hardness, friability, weight variation, wetting time, thickness, water absorption ratio, disintegrating time, uniformity of content and in-vitro drug release. All the tablets had hardness 2.3-3.7 kg/cm2 and friability of all formulations was less than 1%, weight variation and drug content were within official limit amongst all formulations,

The formulation F9 prepared by 6% Ac-Di-Sol showed least disintegrating time of 11sec. and faster dissolution. Formulation F9 was then studied for accelerated stability studies as per ICH guidelines for 60 days that shows no remarkable change in the formulation.

Key words: Angina pectoris, Ac-Di-Sol, Croscarmillose Sodium, Crosspovidone, ICH guidelines

1. Introduction

The concept of MDDDS emerged with an objective to improve patient's compliance. These dosage forms rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration, an attribute that makes them highly attractive for paediatric and geriatric patients. Difficulty in swallowing conventional tablets and capsules is common among all age groups, especially in elderly and dysphagic patients. This disorder of dysphagia is associated with many medical conditions including stroke, Parkinson's disease, AIDS, thyroidectomy, head and neck radiation therapy and other neurological disorders including cerebral palsy. One study showed that 26% out of 1576 patients experienced difficulty in swallowing tablets due to their large size, followed by their surface, shape and taste. Elderly patients may find the administration of the conventional oral dosage forms difficult as they regularly require medicines to maintain a healthy life. Children may also have difficulty in ingesting because of their underdeveloped muscular and nervous systems. The problem of swallowing tablets is also evident in travelling patients who may not have ready access to water. Aforementioned problems can be resolved by means of Mouth Dissolving Tablets (MDTs).

MDTs are known by various names such as "fast-melting, fast-dissolving, oral disintegrating or orodisperse". The European Pharmacopoeia defines the term "orodisperse" as a tablet that can be placed in the mouth where it disperses rapidly before swallowing. Suitable drug candidates for such systems include neuroleptics, cardiovascular agents, analgesics, antiallergics and drugs for erectile dysfunction. MDTs disintegrate and/or dissolve rapidly in saliva; therefore, water is not required during administration. Some tablets are designed to dissolve in saliva within few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity and are more appropriately termed as fast-disintegrating tablets, as they may take about one minute to

disintegrate completely. MDTs offer several advantages over other dosage forms like effervescent tablets, dry syrups and chewing gums/tablets, which are commonly used to enhance patient's compliance. Administering effervescent tablets/granules and dry syrups involve unavoidable preparation that include the intake of water. Elderly patients cannot chew large pieces of tablets or gums and sometimes experience the bitter or unpleasant taste of the drug in the dosage form if the taste masking coat ruptures during mastication.

Advantages of MDDDS

• Ease of administration to patients who cannot swallow, such as the elderly, stroke victims and bedridden patients; patients who should not swallow, such as renal failure patients; and who refuse to swallow, such as paediatrics, geriatric and psychiatric patients .

• Patient's compliance for disabled bedridden patients and for travelling and busy people who do not have ready access to water.

Mouth Dissolving Tablets I: An Overview of Formulation Technology 311Sci Pharm. 2009; 77; 309–326.

• Good mouth feel property of MDDDS helps to change the basic view of medication as "bitter pill", particularly for paediatric patients due to improved taste of bitter drugs.

• Convenience of administration and accurate dosing as compared to liquid formulations.

• Benefit of liquid medication in the form of solid preparation.

• More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and oesophagus which may produce rapid onset of action .

• Pregastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.

• New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of product promotion and patent-life extension .

Ideal Properties of MDDDS

They should,

• Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds.

• Allow high drug loading.

• Be compatible with taste masking and other excipients.

• Have a pleasing mouth feel.

• Leave minimal or no residue in the mouth after oral administration.

• Have sufficient strength to withstand the rigors of the manufacturing process and post manufacturing handling.

• Exhibit low sensitivity to environmental conditions such as humidity and temperature.

• be adaptable and amenable to existing processing and packaging machinery.

• Allow the manufacture of tablets using conventional processing and packaging equipments at low cost.

Various manufacturing techniques for MDDDS include:

1. Lyophilization

2. Moulding

3. Direct Compression

4. Cotton Candy Process

5. Spray Drying

6. Sublimation

7. Mass Extrusion

8. Nanonization

9. Fast Dissolving Films

Desired characteristics and development challenges of ODT

- Rapid disintegration of tablet
- Sufficient mechanical strength
- Avoid tablet size enlargement
- Taste and mouth feel

- . Stability
- . Good packing
- . Good compatibility with development technology
- . Swellability
- . Minimum or no residue in mouth
- . No effect of drug properties on formulation
- . Bioavailability

2. Materials and Methods

Materials

The materials used were: Amlodipine Besylate (obtained as a gift from Lupin Limited, Aurangabad , India), Crossprovidone (Lupin Limited, Aurangabad , India), Croscarmellose Sodium (LobaChemie, Bombay), Ac-Di-Sol (Qualigens Fine Chemicals,Mumbai), Magnesium Stearate (kindly supplied by Unichem, New Delhi), Manitol (All-Wells Chemicals, Chandigarh), orange dry mix fl avor (Lux fl avors,Chennai), Talc (Lupin Limited, Aurangabad , India), Campher (Wockhardt Research Center, Aurangabad)

Preparation Method:

The superdisintegrants (Crossprovidone , Ac-disol, Croscarmillose Sodium) in varying concentration(02%, 04% & 06%) used to develop the tablets. In this study fast-dissolving tablet were prepared by using camphor as sublimating agent. Nine formulations of Amlodipine Besylate containing camphor indifferent proportions were prepared by using Mannitol as a diluent. All the ingredients were passed through # 60mesh separately. The drug and the diluents was mixed in small portion of both each time and blending it to get uniform mixture and set aside. The other ingredients were weighed and mixed in geometrical order, mixed thoroughly with lubricant. The tablets of weight 100 mg were prepared by direct compression technique using 5.3 x 7.6 mm punch in tablet punching machine weighing 100 mg each. After that the compressed tablets are dried for 5 hours for the sublimation of camphor.

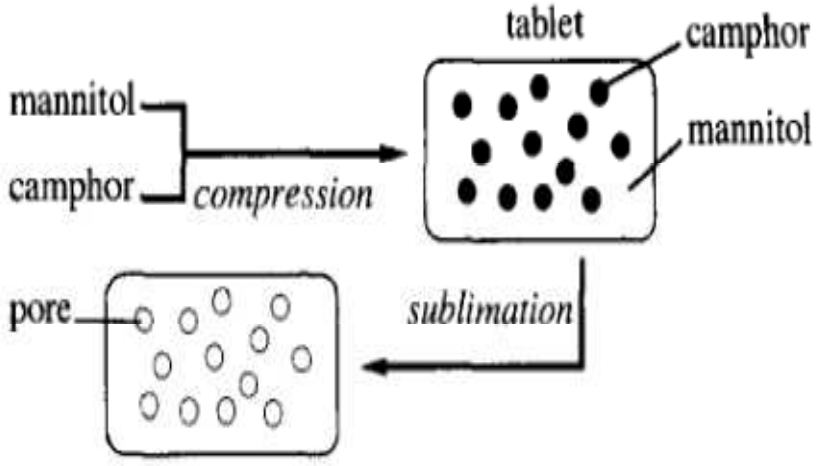

Figure 1: Schematic illustration of the preparation of a high porosity compressed tablet using Manito and Camphor Sublimating agent.

3. Experimental work:

Formulation composition for tablets prepared by Using Various Superdisintegrants

Sr. no.	**Ingredients**	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	**Amlodipine Besylate**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
2	**Crosspovidone**	**2**	**4**	**6**	**-**	**-**	**-**	**-**	**-**	**-**
3	**Croscarmellose Sodium**	**-**	**-**	**-**	**2**	**4**	**6**	**-**	**-**	**-**
4	**Ac-Di-Sol**	**-**	**-**	**-**	**-**	**-**	**-**	**2**	**4**	**6**
5	**Magnesium Stearate**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
6	**Talc**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
7	**Campher**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
8	**Manitol**	**76**	**74**	**72**	**76**	**74**	**72**	**76**	**74**	**72**
	Total Wt. of Tablet	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

4. **Evaluation of Fast Dissolving Tablets**

Formula-tion	Weight variation	Hardness	Friability	Drug content	Wetting time	Water Absorption ratio	Thickness	Disintegration time
F1	2.4±0.51	2.3±0.14	0.43±0.29	97.28	20±0.9	28.91±2.1	3.1±0.5	27±2.1
F2	3.3±0.29	2.6±0.11	0.52±0.13	96.4	21±1.1	39.30±1.9	3.1±0.4	23±2.8
F3	4.1±0.28	3.2±0.15	0.74±0.32	96.86	16±1.7	59.00±1.7	3.0±0.6	18±2.0
F4	2.5±0.35	3.1±0.14	0.33±0.16	97.84	31±1.9	41.23±1.4	2.95±0.5	33±2.2
F5	3.7±0.12	3.2±0.27	0.47±0.25	98.15	23±1.2	58.11±1.2	3.3±0.2	26±2.3
F6	2.2±0.46	3.5±0.26	0.69±0.27	97.73	30±1.7	69.89±1.4	3.1±0.3	32±1.0
F7	3.9±0.23	2.8±0.30	0.37±0.16	96.57	15±0.9	42.92±1.9	3.15±0	17±2.0
F8	2.1±0.15	3.2±0.13	0.52±0.32	98.19	13±1.0	64.47±2.2	2.95±0.2	14±2.5
F9	3.1±0.33	3.7±0.22	0.75±0.33	98.23	10±0.8	81.73±2.4	3.15±0.5	11±2.2

DISSOLUTION STUDY:

Release profile of Amlodipine besilate Orodispersible tablets prepared by sublimation method:

Table 01: Release profile of amlodipine besilate tablets containing crosspovidone.

Time in min	% Drug Release		
	1	**2**	**3**
5	38.78	39.86	41.29
10	46.85	48.44	51.77
15	60.96	65.65	70.91
20	71.24	73.29	79.43
25	87.38	89.27	92.29
30	94.76	95.25	97.00

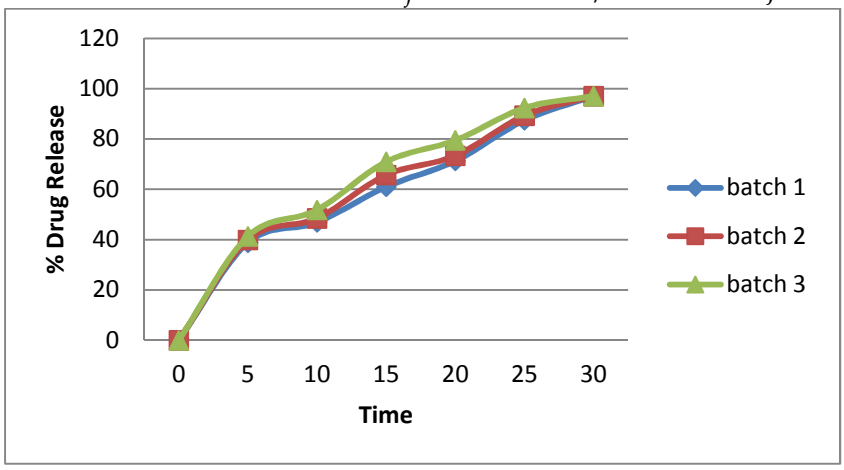

Fig 02: Release profile of amlodipine besilate tablets containing crosspovidone.

Table 02: Release profile of amlodipine besilate tablets containing croscarmellose sodium.

Time in min	% Drug Release		
	4	5	6
5	32.08	36.71	38.38
10	43.21	45.37	49.19
15	53.00	61.18	72.02
20	70.61	72.23	76.70
25	85.09	87.84	90.32
30	91.31	93.20	94.83

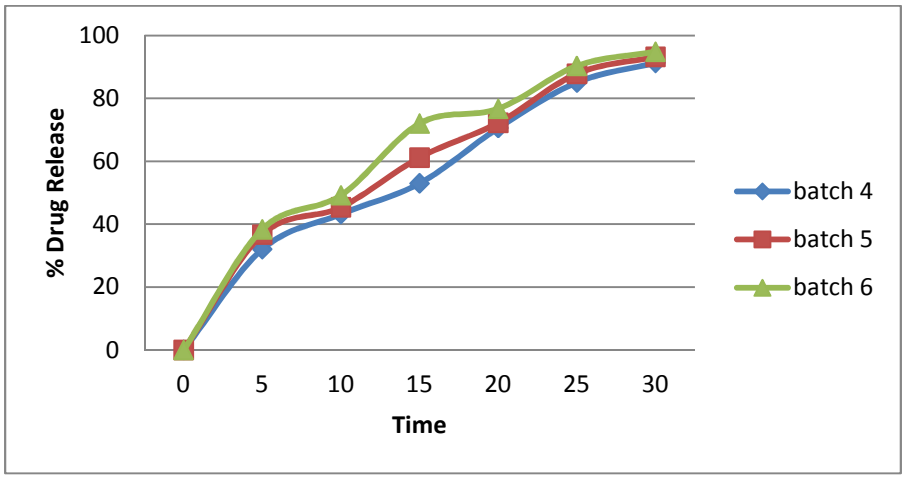

Fig 03: Release profile of amlodipine besilate tablets containing croscarmellose sodium.

Table 03: Release profile of amlodipine besilate tablets containing Ac-Di-Sol.

Time in min	% Drug Release		
	7	**8**	**9**
5	40.72	41.90	42.22
10	48.01	49.52	52.11
15	63.12	69.24	74.21
20	72.10	74.35	81.36
25	89.69	90.81	94.18
30	95.75	96.12	98.23

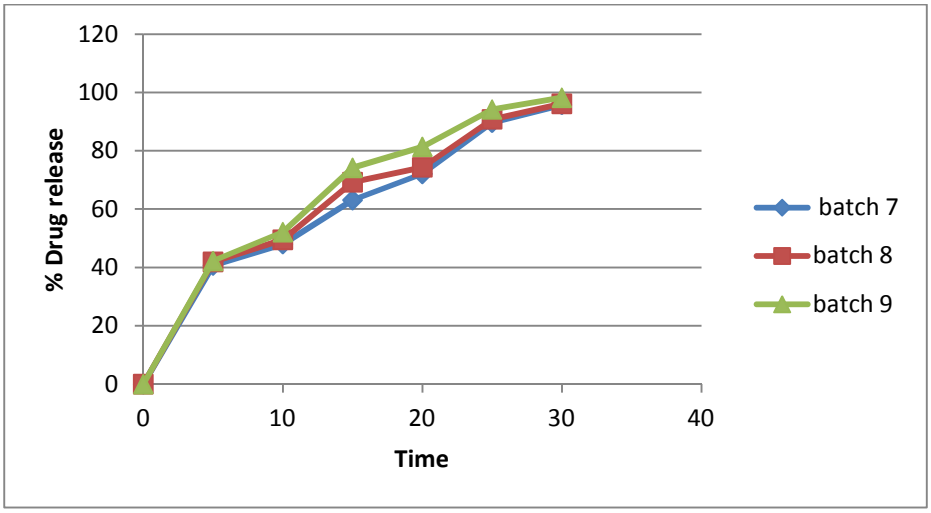

Fig 04: Release profile of amlodipine besilate tablets containing Ac-Di-Sol

Results and Discussion

6.1 Identification of Amlodipine besilate:

The sample of amlodipine besilate procured for study was identified by Infrared spectrum.

6.2 Calibration Curve of amlodipine besilate:

As UV spectrophotometric method was selected for quality control purposes, the λ_{max} was found to be 237.5nm from UV spectrum of amlodipine besilate in methanol. From the standard curve of Amlodipine besilate (table no. 12, 13 & fig.7, 8) it was observed that the drug obeys Beer's law in concentration range of 5 –30µg/ml in

phosphate buffer pH 7.4 & methanol. The linear regression equation generated was used for the calculation of amount of drug.

6.3 Pre-formulation studies:

A) Angle of repose (θ):

The data obtained from angle of repose for all the formulations were found to be in the range of $26^0.28`$ and $30^0.72`$. All the formulations prepared s showed the angle of repose less than 30^0, which reveals good flow property.

B) Bulk density:

Loose bulk density (LBD) and tapped bulk density (TBD) for the blend was performed. The loose bulk density and tapped bulk density for the entire formulation blend varied from 0.507 gm/cm^3 to 0.558 gm/cm^3 (direct compression method) and 0.618 gm/cm^3 to 0.657 gm/cm^3 (sublimation method) respectively.

C) Hausner ratio:

Hausner ratio of entire formulation showed Between 1.14 to 1.26 indicates better flow properties.

D) Carr's consolidation index:

The results of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 13.87% to 20.68%.

6.4 Post compression parameters:

A) Hardness:

Tablet crushing strength, the critical parameter was controlled as the resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage, depends on its hardness. Hence, hardness for all formulation batches prepared was found to be between 2.3 to 3.70 Kg/cm^2. This finding was observed due to constant tablet press setting across all batches, irrespective of weight variation.

B) Friability:

To achieve % friability within limits for an Oro-dispersible tablet is a challenge to the formulator since all methods of manufacturing of Oro-dispersible tablet are responsible for increasing the % friability values. The %

friability values for all formulation batches prepared was found to be between 0.43 to 0.75 % This was also observed due to constant tablet press setting across all batches.

C) Average Weight:

As material was free-flowing, tablets were obtained of uniform weight due to uniform die fill with acceptable variation as per I.P. standards. The weight variation was found in all designed formulations in the range 98 to 102 mg. All the tablets passed weight variation test as the average percentage weight variation was within 7.5% i.e. in the pharmacopoeial limits.

D) Thickness:

Thickness for all formulation batches prepared was found to be between 2.95 to 3.3 mm. This finding was observed again due to constant tablet press setting across all batches, irrespective of weight variation. The standard deviation values indicated that all the formulations were within the range.

E) In vitro Disintegration Time:

Disintegration, the first important step for a drug absorption from a solid dosage form after oral administration was preliminarily focused. It was reported that tablet disintegration was affected by the particle size, the degree of substitution, and extent of cross-linkage. An important factor affecting the disintegration is the tablet hardness and/or the compaction force used in making the tablet hardness. The hardness of the tablet has an influence on the disintegration time as it affects the porosity of the matrix and, accordingly, the ability of water to penetrate through the matrix. All tablets disintegrated rapidly without disc in the IP test especially when used at optimum concentrations of selected superdisintegrants.

The *invitro* dispersion time of Amlodipine besilate prepared by direct compression and sublimation method were found to be in the range of 25 to 53 sec fulfilling the official requirements. Based on the *in vitro* disintegration time, formulation with Ac-Di-Sol were found to be promising and showed a dispersion time of 11 sec respectively. Disintegrating study showed that the disintegrating times of the tablets decreased with increase in the concentration

of croscarmellose sodium, crospovidone .However, disintegration times increased with increase in the concentration Ac-Di-Sol in the tablets.

Results shows that tablets prepared with Ac-Di-Sol superdisintegrant and camphor (sublimation method) showed least disintegration time in comparison with the all other formulations because of their lowest hardness and the porous structure is responsible for faster water uptake, hence it facilitates wicking action of croscarmellose sodium in bringing about faster disintegration.

F) Wetting Time

Wetting time is another important related inner structure of tablet & parameter to water absorption ratio, which needs to be assessed to give an insight into the disintegration properties of the tablets. Wetting time for all formulation batches prepared showed wide variation in the range of 10 to 31 seconds. This wide variation range was observed due to developmental changes in formulation.

Wetting time for all these formulation batches varied in the following increasing order: Crospovidone < Croscarmellose sodium < Ac-Di-Sol.

G) Water absorption ratio:

The formulations prepared by both the technique shows water absorption ratio in the range 29 to 82 % formulations containing only Crospovidone using as superdisintegrant shows lower water absorption ratio when compared to formulations of Ac-Di-Sol using as superdisintegrant, the water absorption ratio also decreases due to less swelling property. It was observed that as concentrations of CCS increases water absorption ratio and it increases due to CCS is made by cross- linking reaction of sodium CMC. This cross linking greatly reduced water solubility of sodium CMC while permitting material to swell and absorbs water many times of its weight.

H) Uniformity of drug content:

The low values of standard deviation indicates uniform drug content in tablets The percent drug content of all the tablets was found to be in the range of 96.44 to 98.23 percent.

I) In vitro dissolution study:

Merely disintegration test is not judicious since all superdisintegrants appear highly efficient, with disintegration times as less than 27 seconds when used in different desired concentrations. However, as discussed above, differences in the particle size generated in the disintegrated tablets could affect drug dissolution since breaking tablets into finer fragments may promote drug dissolution by providing larger total surface areas for drug dissolution to take place.

In case of tablets prepared by direct compression technique the % drug release values increased with increase in the concentration of crosscarmellose sodium, crospovidone and Ac-Di-Sol. The rapid increase in dissolution of amlodipine besilate with the increase in crosscarmellose sodium may be due to rapid swelling and disintegrating tablets rapidly into apparently primary particles. While tablets formulated with Ac-Di-Sol, disintegrate by rapid uptake of water, followed by rapid and enormous swelling into primary particle but more slowly due to the formation of a viscous gel layer. Crospovidone containing tablets rapidly exhibits high capillary activity and pronounced hydration with a little tendency to gel formation and disintegrates the tablets rapidly but into larger masses of aggregated particles. Thus difference in the size distribution generated with different superdisintegrants might have contributed to difference in the % drug release values with the same amount of superdisintegrants in the tablets.

As the method of preparation of tablets changed to sublimation, the dissolution of the drug from the tablets prepared by camphor sublimation method was quicker than those prepared by other method. This may be due to their lowest hardness and the porous structure is responsible for faster water uptake, hence it facilitates wicking action of crosscarmellose sodium in bringing about faster disintegration. All the formulations showed rapid % drug release due to fast disintegration of tablets.

J) Stability studies:

The promising formulations were subjected to short term stability study by storing the formulations at 40°C/75% RH up to three month. The formulations F1 to F9 were selected. After three month the tablets were again analyzed for the hardness, friability, drug content uniformity and dispersion time. Decrease in the disintegration time was observed in tablets prepared by camphor sublimation method. Since during the preparation of tablets by camphor

sublimation method, only 6 hrs at 50°C was used, where as 90 days and 45°C were used during stability studies. No significant change was observed in the drug content of all formulation.

5. Conclusion

In the present work Oral dispersible tablets of Amlodipine besilate were prepared by sublimation methods using superdisintegrants such as Ac-Di-sol, croscarmellose sodium and crospovidone. In sublimation method, camphor is used as subliming agent.

All the tablets of Amlodipine besilate were subjected to weight variation, hardness, friability, *in vitro* dispersion, drug polymer interaction, drug content uniformity, water absorption ratio, wetting time, and *in vitro* drug release.

Based on the above studies following conclusions can be drawn:

- Tablet prepared by sublimation methods were found to be good and were free from chipping and capping.
- Postcompressional parameter (hardness, friability, thickness and drug content) was within the acceptable limit.
- IR spectroscopic studies indicated that the drug is compatible with all the excipients.
- Based on the disintegration time, formulation with croscarmellose sodium were found to be promising and showed a dispersion time of 27 sec, wetting time of 76 and 70 sec respectively, which facilitate the faster dispersion in the mouth.
- The formulation have displayed good water absorption ratio of 56.25 and 60.00%, which indicate better and faster swelling ability of the disintegrants in presence of little amount of water.
- The *in vitro* drug release from mouth dissolving tablets of Amlodipine besilate prepared by sublimation methods were found to be 96.40 to 98.23% respectively within 30 minute. The sublimation method was found to be superior to direct compression method.
- The stability study shows that no significant changes in drug content after three month study.

6. **References**

1. Sameer G, Late, Yi-Ying Yu, Ajay K, Effect of disintegration- promoting agent, lubricants and moisture treatment on optimized fast disintegrating agent. Int J Pharm. 2009; 365:1-11.

2. Chien Y W, Novel drug delivery systems. New York – Marcel Dekker Inc., 2nd ed.1992.

3. Jaysukh J Hirani, Dhaval A Rathod, Kantilal R Vadalia, Orally Disintegrating Tablets: A Review. Tro J. Pharm. Res. 2009; 8 (2): 161-172.

4. D Bhowmik et al, Fast Dissolving Tablet: An Overview J. of Chem. and Pharm. Res. 2009; 1 (1): 163-177.

5. G. Abdelbary et al, The preparation of orally disintegrating tablets using a hydrophilic waxy binder. Int. J. Pharm. 2004; 278: 423–433.

6. Anantha Lakshmi Pallikonda, Ravindar Bairam, M. Motilal, Mekala Shubash Kumar, Formulation and Evaluation of Mouth Dissolving Tablets. Sch. Res. Lib. 2010; 2 (1): 342-346.

7. Tapan Kumar Giri, Dulal Krishna Tripathi And Rana Majumdar, Formulation Aspects in the Development of Orodispersible Tablets: An Overview. Int. J. Pharma. and Pharm. Sci. 2010; 2 (3): 38-42.

8. Mukesh Gohel, Formulation Design and Optimization of Mouth Dissolve Tablets of Nimesulide Using Vacuum Drying Technique. AAPS Pharm. Sci. Tech. 2004; 5 (3): 1-6.

9. Simone Schiermeier, Peter Christian Schmidt, Fast dispersible ibuprofen tablets. Euro. J. Pharm. Sci. 2002; 15: 295–305.

10. Bandari S et al, Orodispersible tablets: An overview. Asian J. Pharm. 2008: 2-11.

11. Suresh B, Rajender K M, Ramesh G, Yamsani M R, Orodispersible tablets: An overview. Asian J. Pharm. 2008: 2-11.

12. Susijit Sahoo et al, Fast Dissolving Tablet: As a Potential Drug Delivery System. Drug Inv. Today. 2010; 2(2): 130-133.

13. Md.Nehal Siddiqui, Garima Garg, Pramod Kumar Sharma, Fast Dissolving Tablets: Preparation, Charactrization and Evaluation: An Overview. Int. J. Pharm. Sci. Rev. Res. 2010; 4 (2): 87-96.

14. S. A. Sreenivas et al, Orodispersible Tablets: New-fangled Drug Delivery System – A Review. Ind. J. Pharm. Educ. Res. 2005; 39(4): 177-181.

15. Dali Shukla, Subhashis Chakraborty, Sanjay Singh, Brahmeshwar Mishra, Mouth Dissolving Tablets I: An Overview of Formulation Technology. Sci. Pharm. 2009; 76: 309–326.

16. Sandipan Kundu, P. K. Sahoo, Recent Trends In The Developments of Orally Disintegrating Tablet Technology. Pharma Times. 2008; 40 (4): 11-20.

17. Nand Pratibha, Vashist Neelam, Singh Amanpreet, Drabu Sushma, Mouth dissolving tablets- A Novel drug delivery system. T. Ph. Res. 2010; 3: 195-202.

18. Rakesh Pahwa et al, Orally Disintegrating Tablets - Friendly to Pediatrics and Geriatrics. Scholars Research Library. 2010, 2 (2): 35-48.

19. Bhupendra G Prajapati and Nayan Ratnakar, A Review on Recent patents on Fast Dissolving Drug Delivery System. Int.J. Pharm.Tech. Res. 2009; 1 (3): 790-798.

20. Manoj Ashok Wagh et al, Techniques used in orally disintegrating drug delivery system International Journal of Drug Delivery 2010; 2: 98-107.

21. P Nand, N Vashist, A Anand, Sushma Drabu, Mouth dissolving tablets- A Novel drug delivery system International Journal of Applied Biology and Pharmaceutical Technology. 2010; 1 (3): 1-7.

22. A Gupta, AK Mishra, V Gupta P Bansal, R Singh, AK Singh, Recent Trends of Fast Dissolving Tablet - An Overview of Formulation Technology. Int. J. Pharm. & Bio. Arc. 2010; 1 (1): 1–10.

23. Martindale, the complete drug reference. 34th edition: 862.

24. Remington's; the science and practice of pharmacy, 20th edition, Lippan cott, Williams & Wilkins, Baltimore, Marryland, 1995; 1364.

25. D.G.Umalkar, Design and Evaluation of Fast Dissolving Tablet of Zopiclone. Int. J. Pharma. Rec. Res. 2010; 2 (2): 86-91.

26. N. G. Raghavendra Rao, Ketan Thube, Ram Pentewar and V.B Suryakar, Comparison of Different Superdisintegrants in Designing of Fast Dissolving Tablets of Metoprolol Tartrate. Int. J. Pharm. Sci. and Res. 2010; 1 (4): 56-66.

27. Debjit Bhowmik, B. Jayakar, K. Sampath Kumar, Design and Characterisation of Fast Dissolving Tablet of Telmisartan. Int. J. Pharma. Rec. Res. 2009; 1 (1): 31-40.

28. Shinde Anilkumar J, Waghule Arun N, Paithane Amol, More Harinath N. Development and characterisation of oral fast dissolving tablet of nifedipine using camphor as a subliming material. Res. J. Pharm, Bio. & Chem. Sci. 2010; 1 (1): 46.50.

29. Parmar R.B., Baria A.H., Tank H.M., Faldu S.D, Formulation and Evaluation of Domperidone Fast Dissolving Tablets. Int. J. Pharm. Tech. Res.2009; 1 (3): 483-487.

30. Suhas M. Kakade et al, Formulation and evaluation of mouth dissolving tablets of losartan potassium by direct compression techniques. Int. J. Res. Pharm. Sci. 2010 1 (3): 290-295.

31. Sheeba FR et al, Formulation and Evaluation of Nifedipine Sublingual Tablets. Asian J. Pharm. & Clinical Res. 2009; 2 (3): 44-48.

32. Uday S Rangole, PS Kawtikwar and DM Sakarkar, Formulation and *In-vitro* Evaluation of Rapidly Disintegrating Tablets Using Hydrochlorothiazide as a Model Drug. Res. J. Pharm. Tech. 2008; 1 (4): 349-352.

33. Ryuichi Narazak, A New Method for Disintegration Studies of Rapid Disintegrating Tablet. Chem. Pharm. Bull. 2004; 52(6): 704-707.

34. Nirav V Patel, Narendra P Chotai, Mayur P Patel, Formulation design of fast -release tablets prepared by melt granulation method. Asian J. pharm. 2008; 22-25.

35. G. Abdelbary et al, Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Int. J. Pharm. 2005; 292: 29–41.

36. Anish Chandy, Sandeep Gupta, Ashish Manigauha, Alok Singh Thakur, Comparative Evaluation of Disintegrants in Orodispersible Tablets of Famotidine. Int. J. Current Pharm. Res. 2010; 2 (3): 44-46.

37. Indhumathi D, Grace Rathnam, Design and Optimization of Orodissolving Tablets of Antidepressant Drug by Superdisintegrants Addition Method. Int. J. Pharma. Sci. Review & Res. 2010; 2 (2): 1-9.

38. Ravi Kumar, M. B. Patil, Sachin R. Patil, Mahesh S. Paschapur, Development And Characterization Of Melt-In-Mouth Tablets Of Haloperidol By Sublimation Technique. Int. J. Pharm. & Pharma. Sci. 2009; 1 (1): 65-73.

39. S Furtado et al, Development and characterization of Orodispersible tablets of famotidine containing a subliming agent. Trop. J. Pharm. Res. 2008; 7 (4): 1185-1189.

40. Ganesh kumar Gudas et al, Formulation and evaluation of fast dissolving tablets of Chlorpromazine HCl. J. Pharma. Sci. & Tech. 2010; 2 (1): 99-102.

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