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Formulation and Evaluation of Antihyperlipidemics Tablets

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A B S T R A C T

The present study is an attempt to develop Orodispersible tablets of Anti hyperlipidemic drug, with superdisintegrates which disintegrates in matter of seconds in the oral cavity, thereby reducing the time of onset of pharmacological action. Direct compression method was used for formulation of orodispersible tablets, microcrystalline cellulose (MCC) and lactose was used as a diluent, Sodium starch glycolate, crosscarmellose sodium and crospovidone were used as superdisintegrates, magnesium Stearate was used as lubricant, neotame as sweetener and orange flavor was used to improve mouth feel. The calibration curve for the estimation of the API was prepared at 247 nm. The method obeyed Beer Lambert's law in the steady range of 3-10µg/ml with a high R^2 value of >0.998 and suggested that the method was reproducible and hence suitable for estimation of API. The API-excipients interaction was studied using FTIR spectroscopy for selected combination of API with different excipients used. The FTIR study reveals that API peaks and API-excipient peaks were not differ, so no API-excipient interactions took place during compatibility study. All the compatibility studies were found to be satisfactory and so formulation trials were started with the selected excipeints. In all formulations the drug release was nearer to 100% within 45 minutes. Formulation T10 showed release (96.09%) in 30 minutes hence T10 was optimized.

Keywords: MCC, Neotame, Crospovidone, Orodispersible tablets

A R T I C L E I N F O

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1. Introduction

The goal of any drug delivery system is to provide a therapeutic amount of drug in the proper site in the body to achieve promptly and then to maintain the desired drug concentration. Oral route is the most preferred route for

administration of drugs. Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing. Tablet is defined as a compressed solid dosage form containing medicaments with or without excipients. According to the Indian Pharmacopoeia Pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drugs or a mixture of drugs, with or without diluents.

Advantages of tablet dosage form

- They are unit dosage form and offer the greatest capabilities of all oral dosage form for the greatest dose precision and the least content variability.
- Cost is lowest of all oral dosage form.
- Lighter and compact.
- Easiest and cheapest to package and strip.
- Easy to swallowing with least tendency for hang-up.
- Sustained release product is possible by enteric coating.
- Objectionable odour and bitter taste can be masked by coating technique.
- Suitable for large scale production.

Disadvantages of tablet dosage form

- Difficult to swallow in case of children and unconscious patients.
- Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.
- Bitter testing drugs, drugs with an objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating. In such cases, capsule may offer the best and lowest cost.

Oral Dispersible Tablets (ODTs)

The main criteria for mouth disintegrating (dissolving) tablet is to disintegrate or dissolve rapidly in oral cavity with saliva in 15 to 60 seconds, without need of water and should have pleasant mouth feel. Orally disintegrating tablets are also called as orodisperse, mouth dissolving, rapidly disintegrating, fast melt, and quick dissolve system. From past decade, there has been an increased demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing day by day. United States Food and Drug Administration (FDA) define orally disintegrating tablets as "A solid dosage form which contain a medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon a tongue".

Advantages of ODTs

- It Bypasses the GI tract and hepatic portal systems, increase the bioavailability of orally administered drugs which can otherwise undergo hepatic first-pass metabolism.
- It improves patient compliance due to the elimination of associated pain with injections; administration of drugs in unconscious or incapacitated patients; convenience of administration as compared to injections or oral medications.
- It provides rapid drug delivery from the dosage forms.
- A relatively rapid onset of action can be achieved as compared to the oral route, and formulation can be removed after discontinuation of therapy.
- The large contact area of the oral cavity contributes to rapid and extensive drug absorption.
- Having rapid onset of action which may leads to an improved bioavailability.
- Patient having difficulty in swallowing tablet can easily administer this type of dosage form.
- Useful for pediatric, geriatric and psychiatric patients.
- Suitable during traveling where water is may not be available.
- Gives accurate dosing as compared to liquids.
- Free of need of measuring, an essential drawback in liquids.

Disadvantages of ODTS

- The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

2. Materials and Methods

Materials

Simvastatin procured from PhEur, Hetero, Microcrystalline Cellulose, Lactose Monohydrate, Butylated hydroxyl Anisole, Citric acid Monohydrate, Carscarmellose sodium, Crospovidone, Sodium Starch Glycolate, Colloidal Silicon Dioxide, Magnesium Stearate, Neotame.

Methods

Antihyperlipidemics tablets were Prepared by direct compression method. Weigh the required amount of API and all excipients. After weighing materials are sifted through different mesh sizes such as followed by sieve no 20, sieve no 40, sieve no 60 to obtain uniform sized particles. BHA, neotame, orange flavor and citric acid are geometrically mixed and pass through sieve no 80, take model drug pass through sieve no 40 and mix with above mixture. Pass diluent through 30# meshes and add equal quantity to above mixture. Then it is subjected to geometrically mixing. The remaining diluents also added after proper mixing and subjected to geometrical mixing. Then add super disintegrating agents and mix for 10 mins. Magnesium stearate passed through sieve no 60 add magnesium stearate to above mixture and lubricate the blend. The tablets were prepared using 8 mm flat faced bevel Edged (FFBE) punches then tablets were compressed.

Evaluation of Tablets

Weight variation test

Tablets were randomly selected from each formulation and their average weight was calculated using digital balance. Individual weight of each tablet was also calculated using the same and compared with the average weight.

Thickness

Thickness was determined for 20 pre weighed tablets of each batch using a digital vernier scale and the average thickness was determined in mm**.** The thickness of the tablet is mostly related to the tablet hardness and can be used as an initial control parameter.

Hardness

The hardness test is performed to measure the tablet strength. Tablet should be hard enough to withstand packing and shipping. Dr. Scheulinger hardness tester was used for the determination of hardness of tablets. The hardness of each tablet was noted and the average hardness was calculated. It is expressed as N (Newton).

Friability

This was determined by weighing 10 tablets after dusting, placing them in the friabilator and rotating the plastic cylinder vertically at 25 rpm for 100 revolutions. After dusting, the total remaining weight of the tablets was recorded and the percent friability was calculated according to

$$\text{Percent friability} = \frac{\text{Initial weight - final weight}}{\text{Initial weight}}$$

Disintegration time

Disintegration time is the time required for a tablet to break up into granules of specified size (or smaller), under carefully specified test conditions. Disintegration time was determined using the disintegration apparatus USP (Electrolab, model no: ED 2AL, Bangalore, India) in water maintaining the temperature at 37 ± 2°C. **h. Wetting time**

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish. 10 ml of water containing amaranth, a water soluble dye is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablets is noted as a wetting time. Six tablets from each batch were taken and evaluated for this test.

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Water absorption ratio

A piece of tissue paper folded twice was placed in a small petridish containing 6 ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighed. Six tablets from each batch were used for this test. Water absorption ratio, R was determined using following equation.

$$R = 10 \times \frac{(W_a - W_b)}{W_b}$$

Where, W_a = Weight of tablet after water absorption.

W_b = Weight of tablet before water absorption.

Dissolution studies

The dissolution test measures the rate of release of the drug from the dosage form. It is usually expressed as extent of dissolution occurring after a given time under specified conditions. *In vitro* release studies are useful for quality control as well as for the prediction of *In vitro-In vivo* correlation. Drug release profile was evaluated *in vitro* using a dissolution test apparatus (Labindia, TDT-08L, Mumbai, India).

Process was carried out in following stage:

Dissolution Parameters:

Medium: Buffer with pH 6.8 containing 0.15%
Sodium dodecyl sulfate.
Volume : 900 ml
Apparatus : USP Type II apparatus (paddle type)
Paddle rotation speed: 75 rpm.
Time : 30 mins
Time points : 5, 10, 15, and 30
Temperature : 37 ± 0.5°C
Samples volume withdrawn: 10ml

Stability studies

Stability study was carried out by exposing the formulation to different conditions including stress condition of temperature and pressure as per ICH guidelines. Generally stability study was done at, 30 /65%RH (for 1, 2, 3 months), 40/75%RH (for 1, 2, 3 months) after the study the samples were checked for physical and chemical properties for any changes and to be within the specifications**.**

3. Results and Discussions

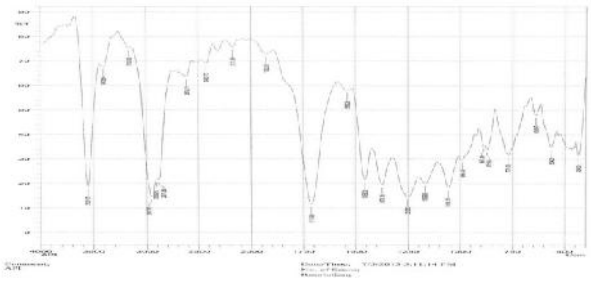

Figure 1: FT-IR Spectra of Simvastatin

By comparing above spectra with the excipients spectra, the major peaks of API were present so it can be concluded that there is no interaction between API and Croscarmellose sodium.

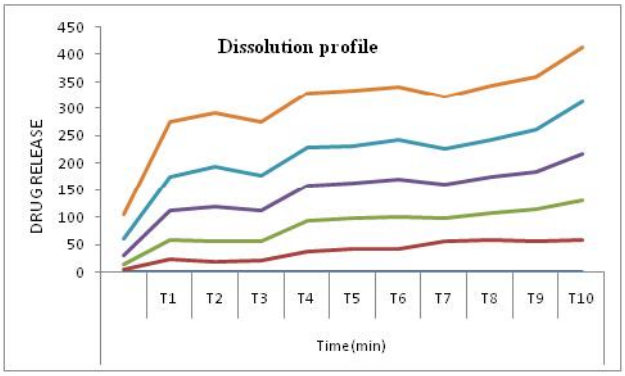

Figure 2: Dissolution profile

Stability or Moisture uptake studies

Tablets of formulation F6 were put on short term stability by packing in HDPE containers in stability chamber at 40^0c±75%RH for the period of one month. It was noted that there was no change in the colour and surface of the tablet .The tablets showed a 99.87 ± 0.63% drug content and 98.12±0.84 % release profile after a period of one month. The results obtained from stability studies for one month showed that all parameters of the formulation including physical parameters were within the specification limit.

Table 1: Ingredients

Ingredients	T1(mg) /Tab	T2(mg) /Tab	T3(mg) /Tab	T4(mg)/ Tab	T5(mg) /Tab	T6(mg) /Tab	T7(mg)/ Tab	T8(mg) /Tab	T9(mg) /Tab	T10(mg) /Tab
Simvastatin	5	5	5	5	5	5	5	5	5	5
Lactose	-	-	-	-	-	-	-	4.00	23.00	1.25
Super Tab 11 SD	86.18	82.18	63.18	-	-	-	-	-	-	-
Avicel pH 101	-	4.00	23.00	-	4.00	23.00	-	-	-	3.75
Avicel pH 102	-	-	-	86.18	82.18	63.18	86.18	82.18	63.18	81.18
BHA	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Carscarmellose sodium	6	6	6	-	-	-	-	-	-	-
Crospovidone	-	-	-	6	6	6	-	-	-	-
SSG	-	-	-	-	-	-	6	6	6	6
Citric acid	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Neotame	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Orange flavor	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Mg stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total	100 mg	100 mg	100 mg	100 mg	100 mg	100 mg	100 mg	100 mg	100 mg	100 mg

Table 2: Pre compression parameters

Formulations	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose	Compressibility index (%)	Hausners ratio	Particle size distribution
T1	0.6178	0.7468	26	17.27	1.208	99.96
T2	0.6672	0.8233	28	18.96	1.233	99.94
T3	0.6196	0.7684	29	19.36	1.240	99.92
T4	0.6483	0.7543	23	14.06	1.169	99.96
T5	0.667	0.7692	25	15.49	1.153	99.95
T6	0.6212	0.7586	27	18.11	1.221	99.91
T7	0.6234	0.7324	23	14.98	1.174	99.98
T8	0.6595	0.7921	26	16.74	1.201	99.96
T9	0.6356	0.7754	28	18.03	1.219	99.92
T10	0.6543	0.7698	27	15.02	1.176	99.91

Table 3: Post compression parameters

Batch No.	Average Weight (mg)	Thickness (mm)	Hardness (N)	Friability (%)	Disintegration time (sec)
T1	101±2%	2.90-2.98	11-15	0.686%	60-90
T2	102±2%	3.01-3.05	15-20	0.521%	60-90
T3	101±2%	2.90-3.01	15-20	0.542%	60-90
T4	98±2%	3.00-3.05	50-80	0.286%	5-10
T5	102±2%	2.88-2.91	50-70	0.209%	5-10
T6	101±2%	2.89-2.91	50-70	0.256%	5-10
T7	102±2%	2.89-2.91	50-70	0.316%	20-30
T8	103±2%	2.89-2.91	50-70	0.231%	20-40
T9	97±2%	2.89-2.91	50-70	0.243%	20-40
T10	99±2%	2.89-2.91	50-70	0.216%	30-40

Table 4: *In-vitro* Dissolution studies of Orodispersible tablets of antiretroviral drug. (F1-F10)

Time(min)	% Cumulative Drug Release									
	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
0	0	0	0	0	0	0	0	0	0	0

5	22.8	19.6	21.3	38.6	41.7	43.4	55.8	58.4	56.3	58.7
10	36.0	37.3	36.3	54.3	56.4	56.9	42.8	48.9	58.5	72.5
15	52.8	62.4	53.2	64.5	65.0	69.7	62.5	68.2	69.1	85.6
30	64.2	73.6	66.8	72.2	68.8	73.3	66.3	67.4	77.0	96.09
45	98.9	98.5	98.3	98.7	99.9	97.4	94.7	98.2	97.9	99.1

4. Conclusion

The present work revealed that sodium starch glycolate showed better disintegration and dissolution property than Croscarmellose sodium and Crospovidone in the formulation of fast dissolving tablets. The effect of diluents and the concentration of the diluents on disintegration and dissolution of Simvastatin were also considered and hence Simvastatin fast dissolving tablet was successfully prepared.

5. References

[1] Adurthi, S., et al., regulatory T cells in a spectrum of HPV-induced cervical lesions: cervicitis, cervical intraepithelial neoplasia and squamous cell carcinoma. Am J ReprodImmunol, 2008. 60(1): p.55-65.

[2] Aqua, K.et.al., SITC: Immunotherapy targeting HPV-E7: preliminary safety from two phase ii studies in women with CIN 2/3 and with recurrent/refractory cervical cancer, 2011.

[3] Basu, P., Petit, R., ADXS-HPV Immunotherapy: preliminary safety data from a phase ii study in recurrent/refractory cervical cancer. AACR Annual Meeting (India), 2011.

[4] Basu, P., Petit, R., Preliminary safety data from phase ii study in recurrent/refractor cervical cancer. ASCO Annual Meeting Chicago IL, 2012.

[5] Borrello, I., and D. Pardoll. 2002. GM-CSF-based celular vaccines: a review of the clinical experience. Cytokine & growth factor reviews 13:185-193. (25)

[6] Bixby, D.L., and J.R.Yannelli. 1998. CD80 expession in an HLA-A2-positive human non-small cell lung cancer cell line enhances tumour-specific cytotoxicity of HLA-A2-positive T cells derived from a normal donar and a patient with non-small cell lung cancer. Int J Cancer 78:685. (33)

[7] Campisi, L., et al., Splenic CD8 alpha dendritic cells undergo rapid programming by cytosolic bacteria and inflammation to induce protective CD8 T-cell memory. Euro Immunol, 2011. 41(6): p.1594-605

[8] Chen, L.,P. Mcf Gowan, S. Ashe, J.V. Johnston, I. Hellstrom, and K.E. Hellstrom. 1994. B7-1/CD80-transduced tumor cells elicit better systemic immunity than wild-type tumor cells admixed with Corynebacteriumparvum. Cancer research 54:5420-5423. (27)

[9] Drake, C.G and E.S Antonarakis, Update: immunological strategies for prostate cancer. Curr Ural Rep, 2010. 11 (3): p. 202-7.

[10] Dunn, G.P., L.J. Old, and R.D. Schreiber.2004. The immunobiology of cancer immune surveillance and immunoediting Immunity 21:137-148. (19)

[11] De Bruyne, L.A., A.E. Chang, M.J. Cameron, Z.Yang, D. Gordon, E.G. Nabel, G.J.Nabel, and D.K.Bishop. 1996. Direct transfer of a foreign MHC gene into human melanoma alters T cells receptor V beta usage by tumour-infilterating lymphocytes. Cancer ImmunolImmunother 43:49-58. (29)

[12] Gajewski, T.F.2007. Failure at the effector phase:immune barriers at the level of the melanoma tumor microenvironment.. Clin Cancer Res 13:5256-5261. (20)

[13] Heike, Y.,M. Takahashi, T. Ohira, I. Naruse, S. Hama, Y.Ohe,T. Kasai, H. Fukumoto, K.J.Olsen, E.E. Podack, and N. Saijo.1997. Genetic immunotherapy by intrapleural, intraperitoneal and subcutaneous injection of IL-2 gene-modified Lewis lung carcinoma cells. International Journal of cancer 73:844-849. (23)

[14] Human Anatomy and Physiology by Ross and Wilson

[15] Immunologic Research 2004; 29/1-3:231-240. (40)

[16] Jabber, S.F., et al., Persistence of high-grade cervical dysplasia and cervical cancer requires the continuous expression of the human papilomavirus type 16 E7 oncogene. Cancer Res, 2009. 69(10): p.4407-14.

[17]. Kim, S.H.e.a., High Efficacy of Listeria-based vaccine against metastic breast cancer reveals dual mode of action. AACR, AACR 2009(69): p.14.

[18] Loddenkemper, C., et al., Regulatory (FOXP3+) T cells as target for immune therapy of cervical intraepithelial neoplasia and cervical cancer. Cancer Sci, 2009. 100(6): p.1112-7.

[19] Maciag, P.C., S. Radlovic, and J. Rothman, The first clinical use of a live-attenuated Listeria monocytogenes vaccine: a Phase 1 safety study of Lm-LLO-E7 in patients with advanced carcinoma of the cervix. Vaccine, 2009.27 (30): p.3975-83.

[20] Marshall, D.J., et al., Induction of Thl-type immunity and tumour protection with a prostate-specific antigen DNA vaccine. Cancer ImmunolImmunother, 2005. 54(11): p.1082-94.

[21] McHugh RS,Nagarjun S, WangYC,Sell KW, Selvaraj P:Protien transfer of glycosylphosphatidylinositol-B7-1 into tumour cell membranes: a novel approach to tumour immunotherapy. Cancer Res 1999; 59:2433-2437. (41)

[22] Nabel, G.J., D. Gordon, D.K. Bishop, B.J. Nickoloff, Z.Y.Yang, A.Aruga, M.J.Cameron, E.G. Nabel, and A.E.Chang. 1996. Immune response in human melanoma after transfer of an allogenic class I major histocompatibility complex gene with DNA-liposome complexes. Proceedings of the national academy of sciences of the United States of America 93:15388-15393. (30)

[23] Nicolle, D.M., et al., Chronic pneumonia despite adaptive immune response to Mycobacterium bevies BCG in MyD88-deficient mice. Lab Invest, 2004. 84(10): p.1305-21.

[24] Noguchi, M., et al., Induction of cellular and humeral immune responses to tumour cells and peptides in HLA-A24 positive hormone-refractory prostate cancer patients by peptide vaccination. Prostate, 2003. 57(1): p.80-92.