J Young Pharm, 2017; 9(3): 332-335
A multifaceted peer reviewed journal in the field of Pharmacy
www.jyoungpharm.org | www.phcog.net

Original Article

Development and Evaluation of Mouth Dissolving Tablets using Natural Super Disintegrants

Venkatalakshmi Ranganathan*[1], Jason Yoong [2]
[1]School of Pharmacy, MAHSA University, Jalan SP 2/7, Bandar Saujana Putra, Jenjarom, Selangor, MALAYSIA.
[2]School of Pharmacy, International Medical University, Bukit Jalil, Kuala Lumpur, MALAYSIA.

ABSTRACT

Objective: To formulate a mouth dissolving tablets of dexamethasone for the use of paediatrics, geriatric patients and also dysphagic patients. **Methodology:** Tablets were formulated by using different types of natural *Super disintegrants* in different concentration such as Guar gum and Xanthan gum. A manual 7 mm single punch tablet compression machine was used to compress the tablet. Powder mixture of 150mg was weighed accurately and added into the die cavity. The prepared dexamethasone MDT tablets were evaluated for its physico-chemical parameters such as thickness, hardness, weight variation, friability, disintegration time, wetting time, *in-vitro* dispersion time, water absorption ratio and also *in-vitro* drug release. **Results:** The FTIR and DSC studies conferred that there is no interaction between dexamethasone and *Super disintegrants*. The dissolution profile of dexamethasone MDT compared with conventional dexamethasone tablet shows improved in % drug release and faster % drug release. An increase in the concentration of *Super disintegrants* showed faster % of drug release and similar % of cumulative drug release. **Conclusion:** Dexamethasone MDT using Guar Gum and Xanthan Gum could be considered as good formulation and delivery system to increase the patient's compliance as the % drug release and disintegration time are much better than conventional Dexamethasone tablet.

Key words: Mouth Dissolving Tablets, dexamethasone, *Super disintegrants*, Rapid disintegration, Dysphagia.

Correspondence :

Dr. Venkatalakshmi Ranganathan, B.Pharm., M.Pharm., Ph.D.

Department of Dosage Form Design, Faculty of Pharmacy, MAHSA University, Bandar Saujana Putra, Jenjarom, Selangor, MALAYSIA.

Email: rvenkatmpharm@gmail.com, lakshmi@mahsa.edu.my

DOI: 10.5530/jyp.2017.9.66

INTRODUCTION

There are quite a number of patients find it hard to swallow tablets as there is physiological changes associated with people especially elderly and pediatrics. Therefore, in order to solve this problem, this project is conducted so that the patients compliance can be improved, a new dosage form convenient for use by geriatric and pediatric dysphagic patients are formulated; reduce the cost of medication for those patients who cannot afford, and also to produce improved products which are available in the market.[1-5]

Dexamethasone, an antiemetic drug which is model drug mostly used as an antiemetic for post-operative and patients undergo chemotherapy. Dexamethasone has a central antiemetic action through activation of glucocorticoid receptors in bilateral nucleus *tractus solitarii*. The dose that was being chosen are 4mg. The chemical formula of dexamethasone is C22H29FO5.

MATERIALS AND METHODS

Dexamethasone, *Croscarmellose* sodium and guar gum were purchased from Sigma-Aldrich MALAYSIA. Other excipients such as *mannitol, sucralose, starch, vanillin* and *magnesium* stearate used and all other reagents used were of analytical grade.

Determination of λ_{max} of Dexamethasone and preparation of calibration curve

Dexamethasone 10 mg was weighed accurately and was completely dissolved in methanol in volumetric flask. The solution was then topped up to 100 ml with methanol to give concentration of 0.1mg/ml. Then, 1ml was pipetted out from the flask and again topped up to 100ml with methanol to give concentration of 1 µg/ml. Aliquots of 1 ml, 2 ml, 3 ml, 4 ml, 5 ml and 6 ml were pipetted out in 10ml volumetric flask.[10,11] The volume was diluted with methanol to give concentration of 0.1, 0.2, 0.3, 0.4, 0.5 and 0.6 µg/ml dexamethasone respectively. A best UV wavelength (λmax) was selected by using spectroscopic scanning run (200-400 nm) with the reference solution and was found to be 239nm.

Formulation of Mouth Dissolving Tablets

Dexamethasone, natural *Super disintegrants*, *mannitol,* magnesium stearate, starch, sucralose and vanillin are being mixed uniformly using geometric trituration and also being weighed accurately prior to compression. Then, a manual tablet compression machine with manual 7 mm single punch was used to compress powder into tablet form. Powder mixture of 150 mg is weighed accurately and added into the die cavity. Lastly, tablets of 150 mg each was produced after compression by the machine.[7-9] The composition of dexamethasone mdt is shown in Table 1.

Compatibility studies[6-10]

Fourier Transform Infrared Spectroscopy

FTIR spectra of the pure drug, excipients, and prepared solid dispersions were obtained on a FTIR. Samples were prepared in KBr disks (2 mg sample in 200 mg KBr). The scanning range was 400–4000 cm−1, and the resolution was 1 cm−1.

Differential Scanning Calorimetry

The DSC thermo gram of pure drug, *Super disintegrants*, and solid dispersions were recorded on a DSC. The samples were weighed and

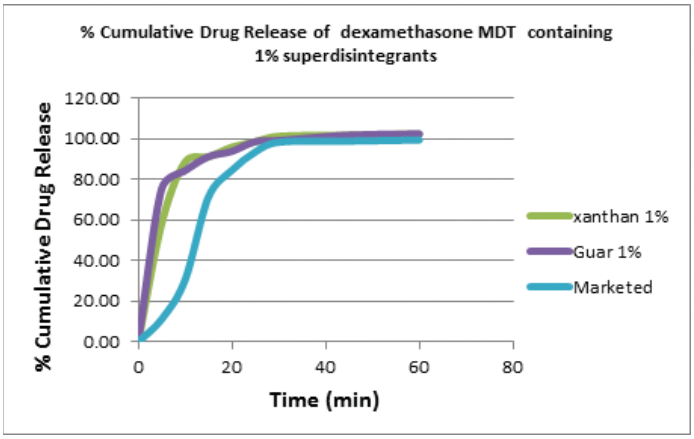

Figure 1: % Cumulative Drug Release of dexamathasone mdt containing 1% xanthan gum, guar gum and marked product

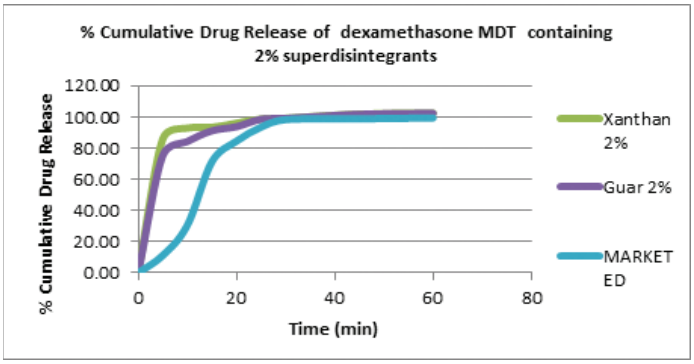

Figure 2: % Cumulative Drug Release of dexamathasone mdt containing 2% xanthan gum, guar gum and marked product

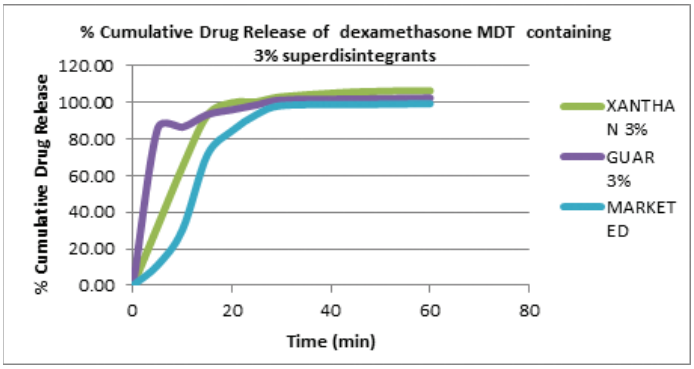

Figure 3: % Cumulative Drug Release of dexamathasone mdt containing 3% xanthan gum, guar gum and marked product

heated in hermetically sealed aluminum pans over a temperature range of 50–300°C.

Physicochemical Evaluation of Mouth Dissolving Tablets [7-11]

Weight Variation

Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. The following percentage deviation in weight variation is allowed as per USP.

Thickness

Vernier calipers was being used to measure the thickness.

Hardness

Monsanto hardness tester Hardness was used to determine the hardness of tablets.

Friability

Ten tablets were accurately weighed and placed in the friabilator and undergo 100 revolutions. Percentage friability was calculated using the following formula.

F= (1-W0/W) × 100, Where, W0 is the weight of the tablet before the test and W is the weight of the tablet after the test.

Disintegration Time

Three tablets were being taken and being placed into each tube of USP disintegration apparatus (distilled water 900 ml at 37°C) as the disintegrating medium. The experiment was being done in room temperature.

Wetting Time

Three tablets were being taken for this test. A petri dish was filled up with 10ml of distilled water. Then, a tissue paper folded twice was placed into the petri dish. The time to for the tablet to wet completely was observed after a tablet was placed on the paper.

In-vitro Dispersion Time

Three tablets were taken for this test. 6ml phosphate buffer solution, pH 6.8 ±0.5°C was prepared before each tablet was being placed. Then, the time for complete dispersion of a tablet was observed.

Water Absorption Ratio

A petri dish was filled up with 10ml of distilled water. Then, a tissue paper folded twice was placed into the petri dish. A tablet was placed on top of the paper and pre-weight of tablets was determined. Then, the tablet which was wet are weighed. Water absorption ratio R, was determined using equation.

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

Where, Wa= weight of the tablet before water absorption Wb= weight of the tablet after water absorption. Three tablets from each formulation were analyzed and standard deviation was determined. The results were shown in table 2.

In-vitro Drug Release [11]

Three tablets from each formulation were being placed into the Electro lab TDT-08L Dissolution Tester. The medium used were 900ml of phosphate buffer pH 6.8 for MDT and 500ml of dilute HCL buffer for conventional marketed Dexamethasone tablets. Temperature was set at 37±0.5 °C; speed at 50 cycles per minute; sample interval was 5min, 10min, 15min, 30min, 45 min and 1 hour; sample volume was 5ml, replacing the aliquots with fresh buffer solution after withdrawing. The drug release and different kinetic models were shown in Table 3 and Figure 1-3.

RESULTS AND DISCUSSION

There was no interaction between the drug and natural *Super disintegrants* according to the results obtained from FTIR and DSC and it shows that drug and polymer are compatible each other.

Thickness found was in the range of 2.5-3.0 mm, hardness was between 2-3 kg/cm^2 and it is important for MDT for achieving fast disintegration, weight variation found to be in between 146.7 mg-129.1 mg, friability

Table 1: Formulation of Dexamethasone Loaded Mouth Dissolving Tablets

Ingredients(mg)	Formulation code					
	XG1	XG2	XG3	GG1	GG2	GG3
Dexamethasone	0.75	0.75	0.75	0.75	0.75	0.75
Mannitol	128.25	126.75	125.25	128.25	126.75	125.25
Sucralose	3.0	3.0	3.0	3.0	3.0	3.0
Xanthan Gum	1.5	3.0	4.5	-	-	-
Guar Gum	-	-	-	1.5	3.0	4.5
Starch	12.5	12.5	12.5	12.5	12.5	12.5
Magnesium Stearate	3.0	3.0	3.0	3.0	3.0	3.0
Vanillin	1.0	1.0	1.0	1.0	1.0	1.0
Total weight	150	150	150	150	150	150
Vanillin	1.0	1.0	1.0	1.0	1.0	1.0

Table 2: Results for Physicochemical Parameters of Dexamethasone MDT

Parameters	XG 1	XG 2	XG 3	GG 1	GG 2	GG 3
Thickness (mm)	2.85	2.73	2.59	2.67	2.72	2.72
Hardness 2-3 (kg/cm^2)	2.90	2.77	2.93	2.93	2.70	2.60
Weight Variation SD<4.5% (mg)	149.1 ± 1.8	149 ± 1.3	149 ± 1.8	147.9 ± 2.2	146.7 ± 3.2	148.6 ± 1.5
Friability <1% (%)	0.57	0.71	0.51	0.98	0.73	0.91
Disintegration Time <60 (sec)	63	58.67	48.67	43.67	39.33	38.33
Wetting Time (sec)	160	126.33	124	53.33	47	45.33
In- vitro Dispersion Time (sec)	119	101.67	59.33	55.67	52.67	34.33
Water Absorption Ratio (%)	0.55	0.58	0.67	0.71	0.83	0.94

Table 3: Kinetics of Drug Release of Dexamethasone MDT

Formulation	Correlation Coefficient, r^2				Kinetic Constant, k	Diffusional Exponent, n	Order of Release
	Zero order	First order	Higuchi Model	Korsemeyer-Peppas Model			
XG 1	-0.696	0.8248	0.579	0.749	0.494	0.202	Fickian Diffusion
XG 2	-1.289	0.7979	0.292	0.967	0.776	0.071	Fickian Diffusion
XG 3	0.018	0.7927	0.324	0.765	0.216	0.447	Fickian Diffusion
GG 1	-0.964	0.955	0.474	0.942	0.631	0.128	Fickian Diffusion
GG 2	-1.000	0.945	0.454	0.868	0.649	0.127	Fickian Diffusion
GG 3	-1.202	0.920	0.342	0.910	0.742	0.084	Fickian Diffusion

between 0.57 %-0.98 %, disintegration time between 38.33 -63 seconds and it shows that MDT can disintegrate quickly without access of water, wetting time between 47-160seconds, *in-vitro* dispersion time between 34.33-119 seconds, water absorption ratio between 0.55 %-0.9 4%. All these parameters are shows that dexamethasone is ideal candidate for delivering as mouth dissolving tablet and all physicochemical parameters were in control limits.

The % drug release for all formulation was between 99.36%-106.39%. The release profile showed that formulation containing natural *Super disintegrants* has higher and faster % drug release compared to conventional Dexamethasone tablets. The higher the concentration of natural *Super disintegrants*, the faster the % drug release and the order of drug release is 1%<2%<3%.

In-vitro drug release was compared with marketed product of conventional dexamethasone tablet and dexamethasone mdt was showing better and faster drug release than marketed product.

In-vitro drug release was compared with marketed product of conventional dexamethasone tablet and dexamethasone mdt was showing better and faster drug release than marketed product. Kinetics of drug release of dexamethasone MDT shows that diffusional exponent, n is less than 0.45 and followed fickian diffusion order of drug release.

CONCLUSION

Tablets and capsules which are currently being considered as the most popular dosage form for oral delivery have some disadvantages to patients undergoing chemotherapy and patients having dysphagia problem. Hence to overcome this problem, current research on Dexamethasone

MDT using Guar Gum and Xanthan Gum could be considered as good formulation and delivery system to increase the patient's compliance as the % drug release and disintegration time are much better than conventional Dexamethasone.

ACKNOWLEDGEMENT

We would like to thank International Medical University for the facilities provided.

CONFLICT OF INTEREST

The author has no conflict of interest.

ABBREVIATIONS USED

MDT: mouth dissolving tablet; FTIR: Fourier Transform Infra-Red Spectroscopy; DSC: Differential Scanning Calorimetry; UV: Ultra Violet Spectroscopy; nm: Nanometer; µg: microgram; ml: *milliliter*; mm: millimeter; USP: United States Pharmacopeia

REFERENCE

1. Indhumathi D, Rathnam G. Design and optimization of orodissolving tablet of antidepressant drug by *Superdisintegrants* addition method. Int J Pharm Sci Rev and Res. 2010;2(2):1-8.
2. Mangal M. *Super disintegrants*: An Updated Review. Int J Pharm Pharm Sci Res. 2012;2(2):26-35.
3. Kumar GP, Nirmala R. Fundamental aspects of *Superdisintegrants*: A concise review. J Global Pharm Tech. 2012;4(2):1-12.
4. Sharma V, Arora V, Ray C. Use of Natural *Superdisintergrant* in Mouth Dissolving Tablet- An Emerging Trend. Int Bull Drug Res. 2010;1(2):46-54.
5. Rao NGR, Patel T, Gandhi S. Development and evaluation of carbamazepine fast dissolving tablets prepared with a complex by direct compression technique. Asian J Pharm Sci. 2009;3(2):97-103. https://doi.org/10.4103/0973-8398.55046.
6. Bhardwaj S, Jain V, Jat RC, Mangal A, Jain S. Formulation and evaluation of fast dissolving tablet of aceclofenac. Intl J Drug Delivery. 2010;2(1):93 https://doi.org/10.5138/ijdd.2010.0975.0215.02017.
7. Mohanachandran PS, Sindhumol PG, Kiran TS. An overview. Int J Pharm Sci Rev and Res. 2011;6(1).
8. Nagar *et al*. Formulation and Evaluation of Piroxicam Fast Dissolving Tablets using Different Natural *Superdisintegrant*. J Drug Deliv and Ther. 2014;4(4):55-9.
9. Yellanki SK, Jagtap S, Masareddy R. Dissofilm: A Novel Approach for Delivery of Phenobarbital: Design and Characterization. J Young Pharm. 2011;3(3):181-8.
10. Vasanthan M, Narayanasamy D. Development of Fast Dissolving Tablets of Nisoldipine by Solid Dispersion Technology using Poloxamer 407 and Poloxamer 188. J Young Pharm. 2016;8(4):341-9. https://doi.org/10.5530/jyp.2016.4.9.
11. Nanam PK, Thadkala K, Sailu C, Aukunuru J. Investigation of various practical techniques to enhance dissolution of ezetimibe from oral tablets: A comparative study. J Young Pharm. 2014;6(1):8-14.

Article History: Submission Date : 24-01-2017; Revised Date : 07-03-2017; Acceptance Date : 17-03-2017.
Cite this article: Ranganathan V, Yoong J. Development and Evaluation of Mouth Dissolving Tablets using Natural Super Disintegrants. J Young Pharm. 2017;9(3):332-5.