Development and Evaluation of Mouth Dissolving Tablets using Natural Super Disintegrants

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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 disso- lution profile of dexamethasone MDT compared with conventional dexamethasone tablet showed improved % 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.

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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.1-3

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 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 λmax 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 1 µg/ml. Aliquots of 1 ml, 2 ml, 3 ml, 4 ml, 5 ml and 6 ml were pipetted out in 10 ml 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 239 nm.

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 studies5-10
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...
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Physicochemical Evaluation of Mouth Dissolving Tablets

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.

Thickenss

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.

\[ F = \left( \frac{1 - W_0}{W} \right) \times 100 \]

Where, \( W_0 \) 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.

\[ R = \left( \frac{W_a - W_b}{W_b} \right) \times 100 \]

Where, \( W_a \) = weight of the tablet before water absorption \( W_b \) = 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

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/cm² and it is important for MDT for achieving fast disintegration, weight variation found to be in between 146.7 mg-129.1 mg, friability

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

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

Figure 3: % Cumulative Drug Release of dexamethasone MDT containing 3% xanthan gum, guar gum and marked product
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 - 160 seconds, in-vitro dispersion time between 34.33 - 119 seconds, water absorption ratio between 0.55 % - 0.94 %.

All these parameters show that dexamethasone is an 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