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Research Article

FORMULATION AND EVALUATION OF LOSARTAN POTASSIUM MOUTH DISSOLVING TABLETS

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ABSTRACT

The concept of MDDDS emerged with an objective to improve patient's compliance. These dosage forms rapidly disintegrate and/or dissolve to release a 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 pediatric and geriatric patients. Difficulty in swallowing conventional tablets and capsules in common among all age groups especially on elderly and dysphasic patients. Elderly patients may find the administration of the conventional oral dosage forms difficult as they regularly require medicines to maintain healthy life. Children may also have difficulty in ingesting because of their under developed muscular nervous system. 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(MDT's). 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 to disintegrate completely.

MATERIALS AND METHODS

MATERIALS

LosartanPotassium, Microcrystalline cellulose (Avicel PH 102), Crosspovidone, Sodium starch glycolate, Cross carmellose sodium, Magnesium stearate, Mannitol.

Preparation of tablets

The formulations prepared were shown in table together with their compositions. The drug, polymer, and diluents were screened through #40 and preblended manually. The lubricant was added and blend was mixed again prior to compression. The tablets blend was directly compressed by using a Elite compression machine.

Evaluation of Tablets

The prepared tablets were evaluated for Hardness,Friability and Weight uniformity.

In-Vitro disintegration time

The disintegration time was measured using a paddle method originally proposed by Sunada et al. The vessel filled with 500ml of 6.8 PH buffer at 37^0c. The paddle was rotated at 100rpm.The tablet was placed inside the sinks and the time at which it passes completely through the mesh of sinker was taken as the disintegration of the tablet.

Drug release studies

Dissolution studies on each formulations of Losartan potassium mouth dissolving tablets were performed in a calibrated three station dissolution test apparatus equipped with paddles employed 900 ml of PH 6.8 buffer as a medium. The paddles were operated to rotate at 75 rpm and the temperature was maintained at 37±1 c through the experiment. Samples were withdrawn at regular intervals up to 45 mins and replaced with equal volume the experiment. Drug content of the samples were determined by Eli co double beam UV

spectrophotometer at 205 nm after suitable dilution of samples. The conventional method of dissolution could be extended to In vitro evaluation of MDT. The dissolution conditions for the reference listed drugs available in USP can be utilized for preliminary in vitro studies to mimic better in in vivo conditions. Apart from the above, multimedia dissolution studies in various buffer solutions of different P^H viz.
0.1N HCL; PH4.5 and 6.8 buffers should be carried out for interpretation of their in vivo performance and pharmaceutical equivalence.

DISCUSSION OF RESULTS

In the present investigation,studies were carried out in the design and development of losartan potassium mouth dissolving tablets using various super disintegrants Sodium starch glycolate, Crosscaramellose sodium, Crosspovidone.
Analytical method used in the present work for the estimation of losartan potassium was well known simple sensitive UV spectrophotometric method. This method was adopted for the estimation of losartan potassium in the MDS tablets and in the invitro studies. The Beer's law obeyed in the concentrations ranges from 0-5µ/ml to maintain accuracy and reproducibility studies. The standard absorbance values at different concentrations were given in Table-1 and the calibration curve was shown in Graph-1&2.
MDT of Losartan potassium was prepared by direct compression using 16 station alight mate miny press. The DC process was used for preparing Oro Dispersible tablets was found to be ideal and easy to prepare the tablets. Super disintegrants such as SSG, CCS,CP exhibiting good flow properties and enabled the process easy. The mannitol is added to the formulation to mask the bitter taste of Losartan potassium which and also enhances the mouth feel. All batches of Oro dispersible tablets were compressed under ideal conditions to minimize the processing variables. Then tablets evaluated for physical parameters such as weight uniformity, hardness and drug content.
The Orodispersible tablets were prepared by direct compression process were having good quality and smooth texture without cracks on the tablets were highly uniform and the results obtained were within the limits.
Losartan potassium release from the Oro dispersible tablets was studied in 0.1N Hcl and 6.8P^H phosphate buffer as the dissolution media for a period of 60 mints. The tablet formulations with sodium starch glycolate released the drug faster when compared with CCS and CP as the disintegrants. As the concentration of super disintegrant increased, the drug release from the Oro dispersible tablet was also increased. The release of the Orodispersible tablets with various super disintegrants were in the increasing order of CP<CCS<SSG. Among the formulations F1 and F2 were found to release the drug at faster rate when compared to the other formulations.
The cumulative % of drug release values for a different formulations were given in the table:6 and dissolution profiles for the formulations were given in the graphs .The In vitro dissolutions parameters such as zero order rate constant, and first order rate constants and dissolution efficiency at 30 mints were calculated for all the formulations and were given in the tables 5 &7.The In vitro disintegration of the Oro dispersible tablets was carried out according to the procedure given by Sunada et al and in vitro disintegration values for all the formulations were given in the table-3. .The in vitro disintegration time was rapid for formulation containing SSG when compared with the other formulations.

SUMMARY

Mouth dissolving tablets are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients.The benefits, in term of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage of choice in the current market.

1. The Losartan potassium was formulated as mouth dissolving tablets using super disintegrants by direct compression.
2. The bitter taste of Losartan potassium was masked by adding Mannitol to the formulations.
3. The physical parameters estimated i.e., weight uniformity, hardness, disintegration time, friability and drug content were highly uniform and were with in the limits of official media.
4. The in vitro drug release studies were conducted for all the Oro dispersible tablets formulations in 0.1 N HCL 6.8 P^H phosphate buffer media.
5. The dissolution of the tablet of the formulation containing SSG as a super disintegrant was rapid than the other tablet formulations.
6. The order of dissolution rate for various Oro dispersible tablets with

various super disintegrants CP<CCS<SSG.

7. All the dissolution parameters estimated and indicated the faster dissolution of drug from Oro dispersible tablet than that of pure drug.

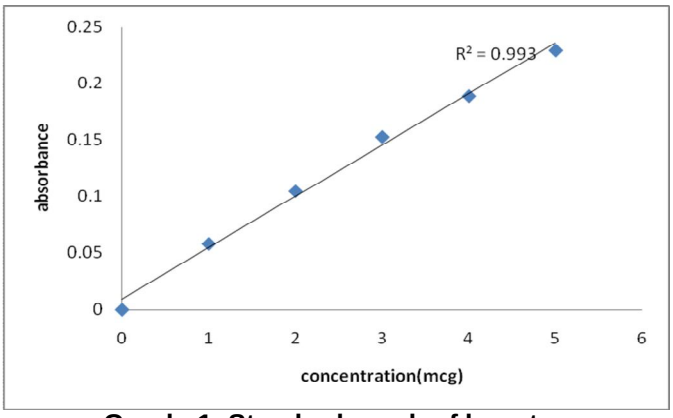
CONCLUSION

Based upon the above conclusions, it may be concluded that Losartan potassium Mouth dissolving tablets prepared with SSG were found to be ideal to increase the dissolution rate. Further these formulations may be subjected to characterization by Differential scanning colorimetry, IR spectroscopy and In vitro disintegration studies, *In vivo* pharmaco kinetic studies and accelerated stability studies to optimize the better formulation.

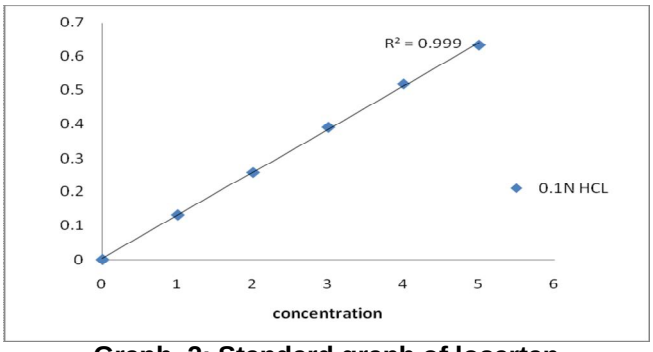
Experimental results

Table 1: Calibration Curve of Losartan Potassium

Concentration (mcg)	Absorbance(nm) 6.8 p^H BUFFER	Absorbance(nm) 0.1 N HCL
0	0.000	0.000
1	0.058	0.131
2	0.125	0.257
3	0.153	0.391
4	0.179	0.518
5	0.230	0.632



Graph. 1: Standard graph of losartan potassium in 6.8Ph buffer



Graph. 2: Standard graph of losartan potassium in 0.1 N HCl

Table 2: Compositions of various Oral Dissolving Tablets of Losartan Potassium

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6
Losartan Potassium	50	50	50	50	50	50
Sodium starch glycolate	40	60	---	---	---	---
Cross povidone	---	---	40	60	---	---
Cross caramellose sodium	---	---	---	---	40	60
Mannitol	30	30	30	30	30	30
Micro crystalline cellulose	78	58	78	58	78	58
Magnesium stearate	2	2	2	2	2	2
Total weight(mg)	200	200	200	200	200	200

Table 3: Physical parameters of tablet evaluation

Formulation	Weight uniformity(mg)	Hardness (kg/cm^2)	Friability (%)	Disintegration time(min)
F1	200±2	3.0-5.0	0.18	1.50
F2	200±2	3.0-5.0	0.19	1.00
F3	200±2	3.0-5.0	0.17	1.55
F4	200±2	3.0-5.0	0.19	1.30
F5	200±2	3.0-5.0	0.18	2.00
F6	200±2	3.0-5.0	0.16	1.45
F7	200±2	3.0-5.0	0.19	3.00

Table 4: Cumulative Percentage release of Losartan Potassium from Mouth dissolving tablets 6.8 P^H Buffer

Time (min)	F1	F2	F3	F4	F5	F6	Pure drug
5	28.94	34.04	53.26	57.38	54.26	54.09	16.13
10	46.48	51.08	62.56	70.94	66.94	69.68	32.26
15	59.82	69.72	75.46	81.26	80.12	84.46	44.39
20	67.38	89.08	87.12	85.82	85.82	87.38	57.52
30	71.88	98.94	91.72	92.86	87.12	91.46	68.65
45	82.16	- -	87.74	98.86	93.26	98.32	79.45

Table 5: *In Vitro* Pharmacokinetic Parameters of Losartan Potassium MDT'S

Formulations	DE30	Zero order constant	correlation coefficient (R^2)	First order constant	correlation coefficient (R^2)
F1	73.O3	2.09	0.851	0.093	0.970
F2	66.06	2.96	0.871	0.09	0.981
F3	60.00	2.25	0.854	0.113	0.988
F4	66.6	1.09	0.873	0.080	0.980
F5	56.06	1.47	0.824	0.078	0.927
F6	63.33	2.95	0.876	0.084	0.971

Table 6: Cumulative Percentage release of Losartan Potassium from Mouth dissolving tablets. In 0.1N HCL

Time (min)	F1	F2	F3	F4	F5	F6	Pure drug
5	50.94	52.04	45.26	47.38	54.26	56.09	16.13
10	68.48	72.08	54.56	58.94	66.94	69.68	35.26
15	81.82	83.72	68.46	72.26	78.12	84.46	58.39
20	86.38	89.08	79.12	83.82	85.82	87.38	67.52
30	91.88	98.94	82.72	89.86	90.12	92.46	80.65
45	92.16	___	91.74	93.86	94.26	96.32	98.78

Table 7: Pharmacokinetic parameters of various mouth dissolving tablet formulations 0.1 N HCl

Formulations	DE30	Zero order constant	Correlation coefficient (R^2)	First order constant	correlation coefficient (R^2)
F1	72.O3	2.09	0.851	0.193	0.970
F2	64.06	2.96	0.871	0.109	0.981
F3	58.00	2.25	0.854	0.145	0.988
F4	64.6	1.09	0.873	0.180	0.980
F5	53.06	1.47	0.824	0.178	0.987
F6	62.33	2.95	0.876	0.124	0.981

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