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EVALUATION OF MOI GUM IN THE FORMULATION OF CONTROLLED RELEASE MATRIX TABLETS USING LOSARTAN POTASSIUM

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Keywords:

Losartan potassium, Moi gum, Controlled release matrix tablets, Polyethylene glycol, Lactose, and dibasic calcium phosphate

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ABSTRACT: Matrix tablets were developed using moi gum for investigating its suitability for the controlled release using losartan potassium as a model drug. Tablets were prepared by direct compression method. Lactose and dibasic calcium phosphate (DCP) were used as channelling agents. *In-vitro* studies were performed in 0.1N hydrochloric acid for the first two hours and pH 6.8 phosphate buffer for the next ten hours. The retardation of drug release was influenced by gum concentration and nature of diluents. The drug release was retarded when compared with dissolution patterns of synthetic polymers like polyethylene glycol (PEG 4000 & PEG 6000). The release rate, extent, and mechanisms were found to be governed by the concentration of the gum and channelling agents. Increased rate and extent of the drug release were found by using a higher content of channelling agent in the matrix due to increased porosity. It was found that type and concentration of channelling agent significantly affect the percentage drug release, release rate constant (K) and diffusion exponent (n). The FTIR studies confirmed that there was no interaction between the drug and moi gum.

INTRODUCTION: Recent decades have seen tremendous strides in the signing of novel dosage forms. But tablets remain an attractive option for pharmaceutical scientists and clinicians because they offer advantages of accurate unit dosing, better patient compliance, ease of large - scale manufacturing, and low production cost [1]. Regular research is going on for the use of natural occurring biocompatible polymeric material in designing of the dosage form for oral controlled release administration [2].

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Biodegradable polymers have been widely used in biomedical applications because of their known biocompatibility and biodegradability. Bio-degradable polymers could be classified into synthetic and natural (biologically derived) polymers. Both synthetic and natural biodegradable polymers have been used for drug delivery, and some of them have been successfully developed for clinical applications. This entry focused on various biodegradable polymers that have been used in the development of drug delivery systems. Advances in organic chemistry and nano / microfabrication / manufacturing methods enable continuous progress in better utilization of a wide range of novel biodegradable polymers in drug delivery [3]. Natural gums are among the most popular hydrophilic polymers because of their cost-effectiveness and regulatory acceptance [4].

Natural gums are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media, so these have been used for the preparation of dosage form. Plant polysaccharides; have been shown to be useful for the construction of drug delivery systems for specific drug delivery [5]. According to the original definition which meant broadly" plant exudates, "the term also encompassed various resins, rubber latex, *etc*. The present definition of gums is somewhat narrower and more specific. It comprises all materials that can be dissolved or dispersed in water to form more or less viscous colloidal solutions or dispersion. Gums have been used as food and also for medicinal purposes by many civilizations. This article emphasizes the one of the natural gum called moi gum for its applicability as controlled release matrix polymer by using model drug losartan potassium.

Moi gum was obtained from the plant *Lannea coromandelica* (Family: Anacardiaceae), which is commonly known as "The Indian Ash Tree" is a deciduous tree which grows up to 14 meters high [6]. It is widely distributed in India, Bangladesh, and some other tropical countries. It is used as a lotion in eruptions, leprous and obstinate ulcers. It is known to cure sprains, bruises, skin eruptions, heart diseases, dysentery, and mouth sores. The decoction of the bark can be used to alleviate a toothache traditionally used to treat impotence [7]. Moi gum is also used as a microencapsulating agent and rate controlling material. This gum has good swelling property and hydrophilic, hence, it can be used as a polymer for the design of controlled release dosage forms.

Losartan potassium is an orally active non-peptide angiotensin - II receptor antagonist used in the treatment of hypertension due to mainly blockade of AT1 receptors [8]. The main limitation of low therapeutic effectiveness is due to narrow therapeutic index, poor bioavailability (25-35%) and short biological half-life (1.5-2.5 h). Conventional tablets should be administered 3-4 times to maintain plasma drug concentration. To increase therapeutic efficacy, reduce the frequency of administration and for better patient compliance in the present research work twice daily controlled release matrix tablets of losartan potassium were prepared by using moi gum in different proportions of drug- polymers and the tablets were evaluated for drug release kinetics and mechanism.

MATERIALS AND METHODS:

Materials: Losartan potassium was received as a gift sample from M/s. Micro Labs Ltd., Pondicherry. Moi gum was purchased from Yarrow Chem Products, Mumbai. Lactose, dibasic calcium phosphate (DCP) and magnesium stearate were purchased from Loba Chemie Pvt. Ltd.

Methodology:

Preparation of Standard Curve of Losartan Potassium: [9] Accurately weighed 50 mg of losartan potassium and dissolved in 100 ml of either 0.1N hydrochloric acid / pH 6.8 phosphate buffer to obtain a solution containing 500 µg/ml of the drug in the respective medium.

The stock solution was suitably diluted to obtain the losartan potassium concentration of 1, 2, 3, 4, 5, 6 & 7 µg/ml with 0.1N hydrochloric acid and 1, 2, 3, 4 & 5 µg/ml with pH 6.8 phosphate buffer and the absorbance was measured at 248 nm against the respective reagent blank *i.e.* 0.1N HCl or pH 6.8 phosphate buffer by using double beam UV visible spectrophotometer (Elico model SL 210). All estimations were done in triplicate, and average values were reported with standard deviation. A standard curve was drawn between absorbance and the concentration and the values of correlation coefficient (r), slope (m) and intercept (c) were calculated.

Pre Compression Parameters: Powders normally flow under the influence of gravity; dense substances are generally less cohesive than lighter ones. Hence, differences in densities of various ingredients may lead to improper mixing and filling during manufacturing of formulation. This results in weight variation and variations in content uniformity of finished products. Hence, determination of density, compressibility index, hausener's ratio and angle of repose of any ingredient will helpful in successful formulation development.

Preparation of Matrix Tablets: The selected gum was used for the preparation of the controlled release matrix tablets of the model drug, losartan potassium using drug-polymer ratios of 1:0.25, 1:0.5 and 1:0.75. **Table 1** 300 tablets were prepared

in each batch by direct compression method because of the good flow properties of the powder blend as per the initial studies carried out. Required quantities of powder were weighed and mixed in a geometric dilution pattern. The final powder blends ready for compression were further evaluated to confirm the flow properties by using compressibility index, hausener's ratio and angle of repose. The powder blends were compressed into tablets by using an Elite 10 station mini press with 8 mm diameter flat round punches with a compression force sufficient to obtain hardness in the range of 4 - 6 kg/cm^2.

For comparison of this selected gum for their suitability for the compression of the controlled release matrix tablets, known established polymers **Table 2** were compared from a synthetic source. Matrix tablets with synthetic polymers were also prepared by direct compression technique using the above-described procedure.

TABLE 1: COMPOSITION OF MATRIX TABLETS OF LOSARTAN POTASSIUM WITH NATURAL GUM

Formulation code	Losartan potassium (mg)	Moi gum (mg)	Dibasic calcium phosphate (mg)	Lactose (mg)	Magnesium stearate (mg)	Total wt of tablet (mg)
MLD1	77	19.25	51.25	-	2.5	150
MLD2	77	38.5	32	-	2.5	150
MLD3	77	57.75	12.75	-	2.5	150
MLL1	77	19.25	-	51.25	2.5	150
MLL2	77	38.5	-	32	2.5	150
MLL3	77	57.75	-	12.75	2.5	150

TABLE 2: COMPOSITION OF MATRIX TABLETS OF LOSARTAN POTASSIUM WITH SYNTHETIC POLYMERS

Formulation code	Losartan potassium (mg)	PEG 4000 (mg)	PEG 6000 (mg)	Microcrystalline cellulose (mg)	Talc (mg)	Magnesium stearate (mg)	Arosil (mg)	Total wt of tablet (mg)
F1	77	19.25	-	205.75	27	14	7	350
F2	77	38.5	-	186.5	27	14	7	350
F3	77	57.75	-	167.25	27	14	7	350
F4	77	-	19.25	205.75	27	14	7	350
F5	77	-	38.5	186.5	27	14	7	350
F6	77	-	57.75	167.25	27	14	7	350

Evaluation of Prepared Matrix Tablets: The prepared matrix tablets were subjected to different quality control tests such as uniformity of weight, hardness, thickness, friability, drug content, and *in-vitro* dissolution studies.

Uniformity of Weight: [10] This test was conducted according to the procedure given in Indian Pharmacopoeia. Randomly twenty tablets were selected, and the average weight was noted. Individual weight of tablets was noted, and the percentage deviation of its weight from the average weight was determined. Prepared tablets pass the test if not more than two of the individual weights deviated from the average weight by more than the 7.5% and none deviate more than twice 7.5% for tablets weighing in the range of >80<250 mg and 5% for tablets weighing >250 mg.

Hardness: [11] Randomly five tablets were selected, and the hardness of each tablet was determined by using Monsanto hardness tester. The tablet to be tested was placed in between the fixed and movable jaw after adjusting the reading to zero. By moving the screw knob, the force on the tablet was gradually increased until the tablet breaks. The pressure required in kg to break the tablet was noted from the scale on the tester.

Thickness: Test was conducted by selecting five tablets randomly; Vernier calipers evaluated the thickness of each tablet. Mean and the standard deviation was calculated.

Friability: [12] Tablets equivalent to the weight of 6.5 g were selected randomly from a batch, and initial weight (w_0) was noted. They were placed in a Roche Friabilator. The chamber was allowed to rotate 100 revolutions. During each revolution, these tablets fall from a distance of six inches to undergo shock. After completion of 100 revolutions, tablets were collected from the

chamber, dedusted and weighed them (w). The loss in weight indicates the friability. The percent loss in weight should not be greater than 1.0% is acceptable. The percent loss in weight or friability (f) was calculated by Eq. 1 given below.

$$f(\%) = \left(1 - \frac{w}{w_o}\right) \times 100 \quad \text{- Eq. 1}$$

Estimation of Drug Content: [13] Ten tablets were randomly selected from each batch, powdered in a mortar individually and the powder equivalent to a dose of the one tablet (77 mg of losartan potassium) was taken into a 100 ml volumetric flask containing 70 ml of pH 6.8 phosphate buffer. The flask was shaken occasionally for 30 minutes, and the volume was made up to 100 ml mark with pH 6.8 phosphate buffer. About 10 ml of the solution was taken and filtered. The filtrate was suitably diluted, and the absorbance was measured at 248 nm against a reagent blank using double beam UV visible spectrophotometer (Elico model SL 210).

***In-vitro* Dissolution Studies:** [14] Dissolution studies were conducted in triplicate for all the prepared tablets in an eight-station dissolution apparatus (Veego) equipped with paddles by using the following dissolution conditions, medium for the first 2 h is 0.1N HCl and medium for the next 10 h is pH 6.8 phosphate buffer, revolutions per minute (RPM) maintained is 75, temperature is 37 ºC. 5 ml of sample was withdrawn for every one-hour interval, and the same amount of medium was replaced to maintain the sink conditions.

Samples were suitably diluted, and drug content was determined by measuring the absorbance at 248 nm as described earlier using double beam UV visible spectrophotometer (Elico model SL 210).

Drug Release Kinetics and Mechanism of Drug Release from the Matrix Tablets: [15-19] The analysis of drug release kinetics and mechanism of drug release from pharmaceutical dosage forms is an important process. The dissolution data were fitted to popular release models such as zero order and first order to determine the rate of drug release and Higuchi's diffusion and erosion equation, to assess the drug release mechanism from the matrix tablets prepared. If the mechanism of drug release is by diffusion it was further characterized by Korsmeyer- Peppa's equation to confirm the diffusion type, *i.e.* Fickian or non-Fickian or anomalous diffusion.

RESULTS AND DISCUSSION:

Standard Curve of Losartan Potassium: The method obeyed Beer's law in the concentration range of 1-7 µg/ml for 0.1 N HCl and 1-5 µg/ml for pH 6.8 phosphate buffers. The 'r' value was found to be more than 0.999 for both the media, which indicated a positive correlation between the concentration of losartan potassium and the corresponding absorbance values. The standard deviation values given in the table were found to be low, which indicated that the method used was reproducible. Thus, the method was found to be suitable in present investigation for estimation of losartan potassium in both the media. The concentration of both the media and corresponding absorbance's **Table 3** are given below. The standard curves are shown below **Fig. 1** and **2** for 0.1N HCl and pH 6.8 phosphate buffer respectively.

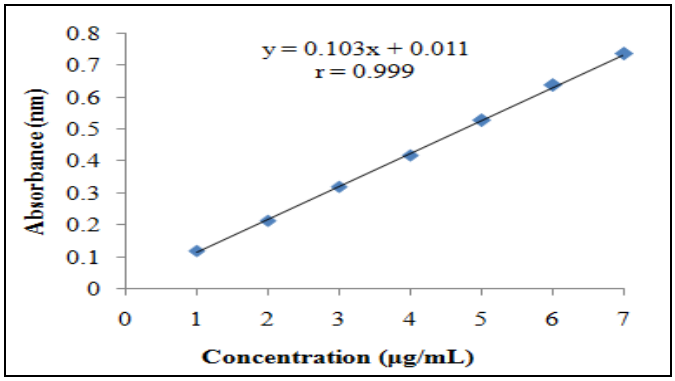

FIG. 1: STANDARD CURVE OF LOSARTAN POTASSIUM IN 0.1N HYDROCHLORIC ACID

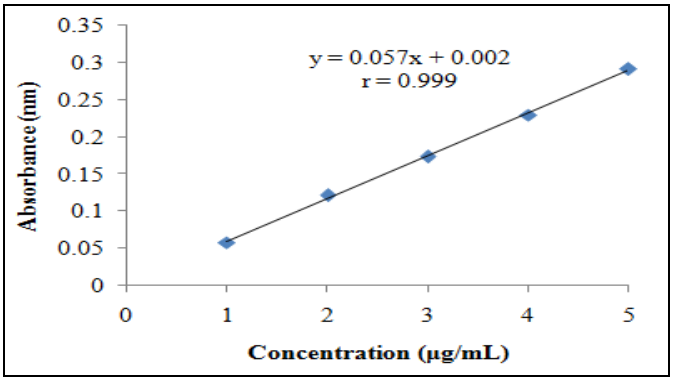

FIG. 2: STANDARD CURVE OF LOSARTAN POTASSIUM IN pH 6.8 PHOSPHATE BUFFER

TABLE 3: STANDARD CURVE DATA FOR LOSARTAN POTASSIUM IN 0.1N HYDROCHLORIC ACID AND pH 6.8 PHOSPHATE BUFFER

Concentration (µg/ml)	Absorbance at 248 nm (mean ± S.D., n = 3)	
	0.1 N HCl	pH 6.8 Phosphate buffer
1	0.121±0.0010	0.058±0.0042
2	0.214±0.0020	0.121±0.0056
3	0.330±0.0010	0.173±0.0078
4	0.419±0.0015	0.230±0.0045
5	0.526±0.0010	0.291±0.0021
6	0.636±0.0026	-
7	0.734±0.0200	-

Flow Properties of the Powder Blend: The powder blends were subjected for evaluation of flow properties **Table 4** and **5** just before compression. Compressibility index ranging 5-20% indicates good flow property of the materials. The angle of repose between 15 - 30º indicates good flow properties of powders.

TABLE 4: FLOW PROPERTIES OF LOSARTAN POTASSIUM POWDER BLEND PREPARED BY USING NATURAL GUM (mean ± S.D., n=3)

Formulation code	Compressibility index (%)	Hausner's ratio	The angle of repose (º)
MLD1	10.07±0.04	1.22±0.41	27.37±0.90
MLD2	9.71±0.62	1.19±0.92	26.59±0.04
MLD3	9.15±0.31	1.16±0.36	27.19±0.12
MLL1	9.75±0.90	1.08±0.68	28.08±0.40
MLL2	8.97±0.26	1.27±0.06	26.46±0.39
MLL3	8.45±0.41	1.19±0.27	28.58±0.31

TABLE 5: FLOW PROPERTIES OF LOSARTAN POTASSIUM POWDER BLEND PREPARED BY USING SYNTHETIC POLYMERS (mean ± S.D., n=3)

Formulation code	Compressibility index (%)	Hausner's ratio	The angle of repose (º)
F1	18.92±0.27	1.20±0.06	27.31±1.54
F2	18.76±0.30	1.19±0.05	27.12±1.43
F3	17.90±0.31	1.23±0.03	26.20±2.10
F4	18.05±0.52	1.23±0.01	18.34±3.13
F5	18.13±0.63	1.45±0.03	18.78±3.10
F6	19.15±0.32	1.21±0.06	19.24±0.12

Evaluation of Tabletting Properties of the Prepared Tablets: The results of uniformity of weight, hardness, thickness, friability, and drug content **Table 6** and **7** for all formulations were calculated. According to IP, the permissible level of deviation is ± 11.25 mg for 150 mg tablet and ± 17.5 mg for 350 mg tablet. As the maximum deviation observed for all the tablets was found to be less than ± 3 mg, and hence, all the tablets passed the test. The hardness of the tablets was in the range of 5.00-6.00 kg/cm^2.

The thickness of tablets was in the range of 2.8 to 4.5 mm. Weight loss in the friability test was less than 1% in all the cases. The drug content in all the matrix tablets was found in the acceptable range of 91.81 to 99.82 and complies with the drug content test (90-110%). Thus the formulated matrix tablets were of good quality, fulfilling the official requirements of the tablets.

TABLE 6: TABLETTING CHARACTERISTICS OF LOSARTAN POTASSIUM MATRIX TABLETS PREPARED BY NATURAL GUM

Formulation Code	Uniformity of weight[a] (mg)	Hardness (Kg/cm^2)	Thickness[b] (mm)	Friability[c] (%)	Drug content[d] (%)
MLD1	149.0±0.59	5.32±0.61	3.1-3.2	0.39±0.12	91.81±0.21
MLD2	150.0±0.75	6.21±0.22	3.0-3.2	0.75±0.42	92.33±0.25
MLD3	151.0±0.12	5.49±0.27	2.8-2.9	0.31±0.46	96.27±0.41
MLL1	150.0±0.45	6.21±0.44	3.0-3.2	0.16±0.20	92.15±0.09
MLL2	149.0±0.89	5.21±0.47	2.8-2.9	0.54±0.39	92.46±0.38
MLL3	151.0±0.33	5.36±0.22	3.0-3.1	0.30±0.52	95.66±0.19

a: Average weight with maximum observed deviation in mg, n=20; b: mean ± S.D., n=5; c: weight equivalent to 6.5 g (44 tablets); d: mean ± S.D., n=10

TABLE 7: TABLETTING CHARACTERISTICS OF LOSARTAN POTASSIUM MATRIX TABLETS PREPARED BY SYNTHETIC POLYMERS

Formulation code	Uniformity of weight[a] (mg)	Hardness[b] (Kg/cm^2)	Thickness[b] (mm)	Friability[c] (%)	Drug content[d] (%)
F1	348.0±0.32	5.7±0.33	3.9±0.17	0.35±0.03	99.82±0.12
F2	353.0±0.43	5.9±0.54	4.0±0.23	0.40±0.04	98.65±0.43
F3	347.0±0.13	6.2±0.41	4.2±0.40	0.32±0.07	98.63±0.21
F4	354.0±0.28	5.7±0.26	4.5±0.34	0.29±0.03	99.21±0.14
F5	349.0±0.45	5.9±0.42	4.3±0.45	0.40±0.04	98.12±0.35
F6	352.0±0.37	6.0±0.38	3.9±0.28	0.31±0.02	98.78±0.25

a: Average weight with maximum observed deviation in mg, n=20; b: mean ± S.D., n=5; c: weight equivalent to 6.5 g (19 tablets); d: mean ± S.D., n=10

***In-vitro* Dissolution Studies for Losartan Potassium Matrix Tablets:** *In-vitro* dissolution studies for losartan potassium matrix tablets were carried out **Table 8** and release profiles of different matrix tablets and corresponding curves **Fig. 3** are shown below.

Initially, tablets were prepared with the lowest concentration of gum, *i.e.* 1:0.25 and drug release was studied. However, the drug release was extended beyond the expected time of 12 h. Hence, channeling agents were incorporated to study their effect on the drug release as well as the consistency of drug release for obtaining the zero order release profile.

The present research work was aimed only for 12 h release profile to avoid the fluctuations going to be caused in 24 h release profile, because of the low therapeutic range of the drug.

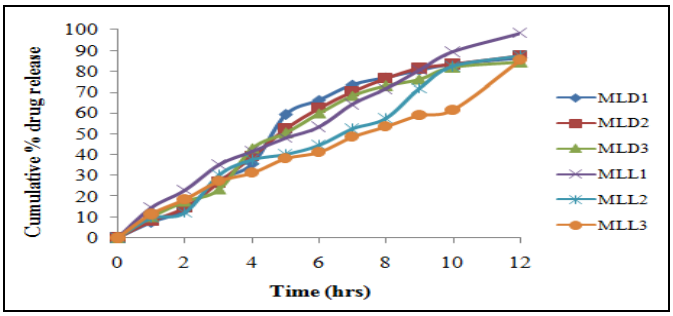

FIG. 3: COMPARATIVE DISSOLUTION PROFILES OF MOI-LOSARTAN POTASSIUM MATRIX TABLETS

TABLE 8: CUMULATIVE PERCENT DRUG RELEASED *vs.* TIME OF MOI-LOSARTAN POTASSIUM MATRIX TABLETS

Time (h)	Cumulative % drug released (mean ± S.D., n=3)					
	MLD1	MLD2	MLD3	MLL1	MLL2	MLL3
		DCP			Lactose	
1	07.44±0.26	08.23±0.94	10.15±0.56	14.62±0.44	09.61±0.18	11.44±0.10
2	13.26±0.13	14.59±0.54	17.56±0.28	22.79±0.22	12.12±0.26	18.50±0.36
3	27.54±0.49	26.59±0.81	23.32±0.59	35.31±0.17	30.26±0.42	27.26±0.42
4	35.69±0.12	39.35±0.15	43.03±0.18	41.68±0.71	37.45±0.15	31.24±0.16
5	59.14±0.56	52.33±0.49	50.29±0.26	48.12±0.14	40.24±0.73	38.18±0.22
6	66.12±0.71	62.31±0.27	59.74±0.31	53.16±0.56	44.47±0.21	41.24±0.58
7	73.59±0.14	70.11±0.47	68.14±0.54	64.13±0.61	52.20±0.32	48.43±0.82
8	77.12±0.49	76.55±0.25	72.85±0.12	71.46±0.22	57.32±0.47	53.32±0.62
9	80.56±0.18	81.26±0.75	76.11±0.89	80.51±0.47	71.56±0.42	58.86±0.56
10	83.23±0.46	83.25±0.15	81.77±0.14	89.17±0.61	82.32±0.37	61.37±0.63
12	86.45±0.31	87.54±0.94	84.32±0.11	98.25±0.55	87.59±0.24	85.35±0.67

Losartan potassium released from the matrix tablets formulated was affected by diluents. In the present work water soluble and water insoluble diluents were used. In case of soluble diluent like lactose, when the tablet is getting exposed to dissolution medium the soluble diluents gets dissolved in the dissolution medium and pores are created through which the dissolution medium penetrates in to the core of the tablet thereby enhancing the faster diffusion of the drug, whereas in case of dibasic calcium phosphate, because it is an insoluble diluent the lag time for penetration of the liquid is more, hence, the drug release is retarded.

As the goal of the present investigation is to complete the drug release uniformly with zero order, soluble diluent played its role in making it uniform drug release compared to the insoluble diluent. Hence, lactose is more suitable for water-soluble drug compared to dibasic calcium phosphate.

From the dissolution studies it was observed that among all formulations, MLL1 showed near 100% drug release throughout 12 h. Hence, among different ratios employed in the present research work, the drug: polymer ratio of 1:0.25 showed optimized release, so it was concluded that the formulation with low concentration of gum and high concentration of diluent was more suitable for the formulation of controlled release matrix tablets for water-soluble drug like losartan potassium.

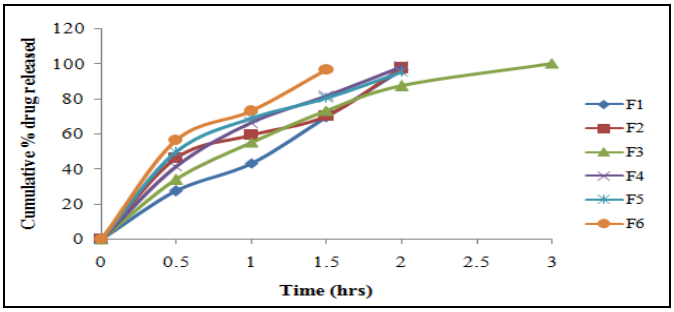

FIG. 4: COMPARATIVE DISSOLUTION PROFILES FOR FORMULATIONS F1 –F6

In case of losartan potassium matrix tablets prepared with synthetic polymers, dibasic calcium phosphate and lactose showed poor tableting characteristics. Hence, they were replaced with microcrystalline cellulose however the drug release is completed within three hours **Table 9** with same ratios of polymers, whereas in case of natural polymers the drug release was extended up to 12 h, hence, further comparisons were not made. Dissolution graphs **Fig. 4** are shown below. Hence, the usage of natural polymer in the preparation of matrix tablets is the better choice to control the drug release throughout 12 h. Commercial formulations with this dose are not available, so we have not compared with commercial tablets.

TABLE 9: DRUG RELEASE PROFILES OF LOSARTAN POTASSIUM MATRIX TABLETS PREPARED BY USING SYNTHETIC POLYMERS

Formulation code	Time (h)				
	0.5	1	1.5	2	3
F1	27.21±0.23	43.17±0.39	69.27±0.05	96.11±0.17	-
F2	46.25±0.28	59.17±0.46	70.21±0.11	97.30±0.40	-
F3	33.75±0.29	55.15±0.20	73.12±0.16	87.25±0.26	99.91±0.04
F4	41.36±0.35	66.17±0.47	81.39±0.55	98.27±0.76	-
F5	49.54±0.03	68.72±0.21	80.14±0.05	95.26±0.33	-
F6	56.14±0.43	73.24±0.02	96.47±0.65	-	-

Drug Release Kinetics of Matrix Tablets: Analysis of release data as per zero order and first order kinetic models indicated that the rate of drug release from the tablets followed first-order kinetics in case of DCP as a diluent, **Table 10** whereas zero-order kinetics in case of lactose as diluent.

Drug Release Mechanism of Matrix Tablets: When the release data was analyzed as per Higuchi's diffusion equation, the release was observed by a diffusion mechanism. To confirm the further type of diffusion, *i.e.* Fickian or non-Fickian data was analyzed with Korsmeyer- Peppa's equation. The release exponent 'n' was in the range 0.71 - 0.89 with all the matrix tablets indicating non - Fickian (anomalous) diffusion with erosion.

Release mechanisms **Table 11** are summarized below. As the moi gum proportion (%) in the matrix tablets was increased, the release rate was decreased in both the series formulated using lactose or DCP as diluent.

TABLE 10: CORRELATION COEFFICIENTS (r) VALUES OF DRUG RELEASE KINETICS OF MATRIX TABLETS OF LOSARTAN POTASSIUM USING DCP AND LACTOSE AS DILUENTS

Formulation code	Zero-order		First order	
	k_0 (mg/hr)	r	k_1 (hr^{-1})	r
MLD1	4.12	0.8545	0.092	0.9651
MLD2	3.90	0.8942	0.082	0.9835
MLD3	3.77	0.9015	0.075	0.9789
MLL1	8.165	0.9871	0.207	0.8945
MLL2	7.401	0.9798	0.198	0.9136
MLL3	4.510	0.9814	0.124	0.8654

TABLE 11: CORRELATION COEFFICIENTS (r) VALUES OF DRUG RELEASE MECHANISMS OF MATRIX TABLETS OF LOSARTAN POTASSIUM USING DCP AND LACTOSE AS DILUENTS

Formulation code	Higuchi	Erosion	'n' value from Peppa's
	r	r	equation
MLD1	0.9500	0.9542	0.82
MLD2	0.9640	0.9766	0.79
MLD3	0.9687	0.9764	0.71
MLL1	0.9974	0.9784	0.89
MLL2	0.9187	0.9617	0.89
MLL3	0.9284	0.9808	0.76

Drug-Excipient Compatibility Studies: Generally drug-excipients compatibility studies were carried out for physical mixtures of drugs and excipients as per ICH guidelines. However, there is the possibility of drug-excipient incompatibility during compression due to heat and other processing

variables rather than a physical mixture. Hence, compatibility studies were carried out for matrix tablets instead of a physical mixture. For other polymers also compatibility studies were not done because these polymers were earlier reported their suitability with losartan potassium.

The technique used was Fourier transform infrared spectroscopy (FTIR) according to the procedure given in previous sections.

Fourier Transform Infrared Spectroscopy (FTIR): Pure moi gum, losartan potassium, and optimized matrix tablet formulation MLL1 were subjected to FTIR spectroscopic analysis, to ascertain whether there is any interaction between the drug and the polymers used. The obtained characteristic peaks **Fig. 5** of losartan potassium were compared with the peaks obtained for their matrix tablet formulation MLL1. The characteristic bands of losartan potassium **Table 12** were identifiable and there was no major shift in them when combined with polymers used in the preparation of matrix tablet. This indicates that the drug was intact and had not reacted with the excipients used in the formulations and hence, they are compatible.

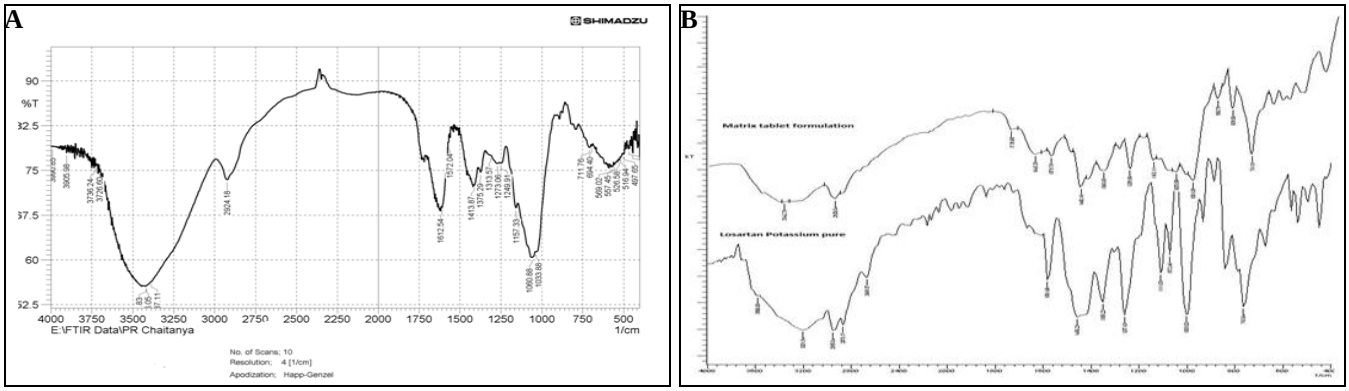

FIG. 5: FTIR SPECTRA OF (A) PURE MOI GUM (B) PURE LOSARTAN POTASSIUM AND OPTIMIZED FORMULA (MLL1)

TABLE 12: FTIR SPECTRAL DATA OF LOSARTAN POTASSIUM AND MATRIX TABLET FORMULATION (MLL1)

Functional groups	Wave number of pure drug (cm^{-1})	Wave number of formulation (cm^{-1})
C-Cl	763.84	761.91
Ar-H	2955.04	2928.04
C-N Stretching	1257.63	1259.36
N=N Stretching	1581.68	1579.75
C-O primary alcohol	1072.46	1070.53
C=C Stretching	1458.23	1460.16
OH Stretching	3201.94	3342.75

CONCLUSION: Matrix tablets of moi gum were prepared in different concentrations. All the formulations were showed good tableting properties. Among different concentrations of gum (1:0.25) were able to show the better-controlled release of losartan potassium from matrix tablets over 12 h. The drug release was enhanced by using channeling agents like lactose and DCP. Among these two channeling agents lactose was showed better enhancement and controlled drug release. The drug release kinetics and mechanisms were evaluated. Compatibility studies were carried out for optimized formulations and the results proved that there was no interaction between drug and polymers.

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