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Assessment of Delonix Regia seed Gum in The Formulation Development of Sustain Release Tablet of Diclofenac Sodium

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Abstract : Objective: The purpose of this investigative research work was to assess the release retardant properties of Delonix Regia seed gum in formulation & evaluation of Diclofenac Sodium Sustain release tablet. This work is in conformity with the exploration of natural polymers to make formulation cost effective & compatible.
Methods & Material: The polymer was extracted from seeds of Delonix Regia& evaluated. Drug-Excipient compatibility was established using FT-IR. Sustained release matrix tablets of Diclofenac Sodium were prepared by wet granulation method. Granules were evaluated for parameters like bulk density, tapped bulk density, compressibility index and angle of repose. The compressed tablets were evaluated for uniformity of weight, hardness, friability, thickness, content uniformity, In-vitro dissolution.
Result: Assessment of release profile enables one to know that amount of drug release from the formulation F3 & F4 upto 10hrs ranged between 50-70%. While, F1 & F2 indicating complete drug release within 10 hrs at low concentrations of DRSG and F5-F8 indicating incomplete drug release at high concentrations of DRSG. Poly Ethylene glycol was used as a channeling agent along with Delonix Regia polymer to improve drug release.
Conclusion: The assessment of dissolution profile of tablets indicates that 15–25 % concentration of DRSG showed good drug release. Combination of channeling agents like PEG was used for modulating the release profile. It was found that 3-5% concentration of PEG showed desirable change of drug release.
Key Words : Sustain release, Matrix tablet, Diclofenac sodium, Delonix Regis Seed Gum, Polymer.

Introduction

Oral route of administration is the most preferred route for administration. Tablets are the most popular oral dosage form and preferred by the patients and physician as well. In long-term therapy for the treatment of chronic diseases,a conventional tablet is required to be administered frequently and therefore associates several disadvantages with them. [(1)] Sustained release drug delivery system aimed at controlling the rate of drugrelease as well as maintains desired plasma concentration of the drug that is therapeutically effective and non-toxic for extended period of time, thus achieving better patient compliance and allowing a formulation scientist to use less amount of drug and avert the incidence of adverse effects. The rationale for development of a sustained release formulation of a drug is to enhance its therapeutic benefits, minimizing its toxic effects.[(2, 3)]The immense progress witnessed in region of design and developments of new drug delivery systems were predominantly incentivized by exploration in polymer science. The need to find a new polymer for the growing research efforts in drug delivery provided the impetus for the development of a variety of new polymers. Consistently accelerating research and development in polymer science has played a vital role in the progress of most

controlled release techniques. In the past decades, there has been conspicuous increase in interest in these technologies, as it is shown by the rising number of publications and patents in the field of controlled drug release systems using semi-synthetic as well as naturally occurring polymeric materials.[(4)]Plant products can serve as a better source of polymers as an alternative to synthetic products. Plants are non polluting renewable resources for sustained supply of affordablepharmaceutical products. We have a number of plant based pharmaceutical excipient like natural gums. Natural materials have been attracting plethora of scientist in the field of drug delivery because they are easily available, cost effective, eco-friendly, capable of chemical modifications, potentially degradable under natural or physiological conditions and compatible due to their natural origin .[(5)]The model drug Diclofenac has analgesic, antipyretic and anti-inflammatory activities. It is a potent relatively non-selective cyclooxygenase inhibitor and its potency is greater than that of Indomethacin, naproxen, or several other agents.[(6, 7, 8)]Polysaccharides are the choice of materials among the hydrophilic polymers used, because they are nontoxic and acceptable by the regulating authorities. The various natural Polysaccharides so far used in various drug delivery applications are cellulose ethers, Gum karaya, Pullulan gum, Gellan gum, xantham gum, locust bean gum, guar gum, *okragum,* olibanum gum tamarind seed gum and Delonixregia seed. [(9)]*Delonixregia* used in treatinggastric problems, body pain, and rheumatic pains of joints [(10)]so by taking all these factors in consideration DRSG polymer was used for the preparation of matrix tablets and it's conc. in the formulations ranging from 5-40% of the total tablet weight was used. Matrix tablets were prepared by wet granulation method. The excipient like lactose, microcrystalline cellulose and dibasic calcium phosphate were incorporated in tablet matrix system, Formulations without channeling agents and with channeling agent (PEG 4000) were formulated. All the formulations were evaluated for various parameters. Dissolution of drug from tablet was studied by various models. The best fit model representing the mechanism of drug release from the matrices was of zero order. This is further confirmed by Korsmeyer–Peppas model; indicating that two or more mechanisms for drug release are involvedi.e. diffusion, erosion, and chain relaxation.

Material and Method

Materials:

Diclofenac was a gift sample from Micro Lab Ltd Bangaluru & Dicalcium Phosphate from Blue Cross Lab. Ltd., Nasik. Polyvinylpyrrolidone, lactose, talc and magnesium stearate were purchased from S. D. Fine Chemicals Ltd (Mumbai, India). All other ingredients were of analytical grade.

Methods:

Isolation of polymer&Characterization of DRSG[(11)]

The seeds of Delonix regia plant were collected and seeds (500 g) were boiled in the distilled water for 3 h until the seedkernels were swelled which was then isolated. The gum part was separated from they ellowish dicotyledons. The gum portion was dried in an oven at 45°C for 12 h and then was pulverized. The resulting powder was then passed through 60 # sieve.The powder was insoluble in maximum solvents except distilled water. The loss on drying, heavy metal content, and all were within official limits. The angle of repose was found to be in between 26 and 30 for the DRSG, indicated that the powder is having good flow property. The Carr's index and Hausner's ratio indicated that the powder is having good flow property and compressibility. Also DRSG showed good swelling index, hydration capacity and water retention capacity. The entire result showed that the DRSG followed swelling type of action

Table 01: Physicochemical properties of DRSG

Parameter	**Results**
Solubility	Insoluble in maximum solvents except distilled water
Loss on drying (%)	5.7
Heavy metals	Not more than 10 ppm
Density (g/ml)	Bulk- 0.4551 ±0.02071
	Tapped- 0.6004±0.02122
Carr's index (%)	24.13±4.4461

Hausner's ratio	1.32±0.07510
Angle of repose (**θ**)	27.65±0.87
Acid value	56.1
Saponification value	93.95
Swelling Index (%)	165.18±8.83
Water retention capacity (ml)	2.48±0.1571
Viscosity(cps)	137±5.5677
Moisture sorption capacity (%)	5.33±0.5773
Hydration capacity	0.4366±0.02081

Drug-Excipient Compatibility Study

FT-IR spectroscopy was used to elucidate the molecular interaction between polymer and drug.

Formulation of Sustained Release Matrix Tablet

DRSG polymer was used for the preparation of tablets and their conc. in the formulations ranging from 5-40% of the total tablet weight was used. Matrix tablets were prepared by wet granulation method as per formula given in Table 02. Initially all the ingredients along with the drug were weighed accurately and passed through 60# sieve. The ingredients and the drug were then mixed in a mortar by geometric progression for a period of 10-15 mins. Distilled water was used as a granulating agent. The wet granules were dried at 50°C for 3 h. the dried granules were passed through 20# sieve and lubricated using magnesium stearate (1%, w/w) and talc (1%, w/w). The resultant granules were compressed in karnavati tableting machine using 8-mm biconvex punches [(12)]

Table 02: Compositions of matrix tablets of Diclofenac sodium for formulations (F1-F8)

Ingredients(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Diclofenac	100	100	100	100	100	100	100	100
DCP	98	86.75	75.5	64.25	53	41.75	30.5	19.25
DelonixRegia(%)	11.25 (5%)	22.5 (10%)	33.75 (15%)	45 (20%)	56.25 (25%)	67.5 (30%)	78.75 (35%)	90 (40%)
PVP(K-30)	11.25	11.25	11.25	11.25	11.25	11.25	11.25	11.25
MagnesiumStearate	2.25	2.25	2.25	2.25	2.25	2.25	2.22	2.25
Talc	2.25	2.25	2.25	2.25	2.25	2.25	2.25	2.25
Total	225	225	225	225	225	225	225	225

Effect of channeling agents on the release rate

Test formulations were formulated for evaluation of the PEG 4000 over the dissolution of the drug from matrix tablet. Formulations without channeling agents and with channeling agent (PEG 4000) were formulated. The procedure for preparation of the tablets is similar to the preparation method of above formulations.

Table 04: Compositions of matrix tablets of Diclofenac sodium for PEG 4000 containing Formulations (C1- C3)

Ingredients(mg)	**C1**	**C2**	**C3**
Diclofenac Sodium	100	100	100
DCP	75.5	68.75	64.25
DelonixRegia(%)	33.75(15%)	33.75(15%)	33.75(15%)
PEG 4000	-	6.75 (3%)	11.25(5%)
PVP(K-30)	11.25	11.25	11.25
Magnesiumstearate	2.25	2.25	2.25
Talc	2.25	2.25	2.25
Total	225	225	225

Results and Discussion

Formulation of Sustained Release Matrix Tablet

The prepared hydrophilic matrix tablets were evaluated for various parameters. Table 06 gives the results of the evaluation parameters with their standard deviation values.

Table 06: Evaluation data for matrix tablets for formulations F1-F8

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Content Uniformity (%)
F1	225.85±5.5	3.76±0.052	7.21±0.52	0.325	99.01
F2	226.1±3.6	3.82±0.047	7.16±0.18	0.278	98.76
F3	226.3±4.5	3.72±0.050	7.67±0.55	0.398	98.56
F4	225.25±4.2	3.80±0.052	7.86±0.50	0.305	98.70
F5	225.9±3.8	3.65±0.052	7.83±0.32	0.220	101.22
F6	226.4±2.6	3.72±0.042	7.66±0.42	0.341	98.85
F7	225.3±4.6	3.66±0.052	8.83±0.24	0.265	100.34
F8	226.2±3.7	3.78±0.041	8.66±0.08	0.309	99.04

All values are expressed as mean± SD, n=3

In-Vitro drug release profiles

Table 7 &8 gives the results of the In-vitro dissolution data with their standard deviation values.

Table 7:In-vitro dissolution data of matrix tablets for formulations F1-F4

Time(Hr)	Formulations(% Cumulative drug release)			
	F1	F2	F3	F4
1	0.145±0.065	0.407±0.549	0.70±0.48	0.038±0.04
2	3.72±1.478	3.13±1.31	2.35±0.14	1.19±0.81
3	11.09±0.851	9.89±1.33	11.59±0.40	9.14±0.99
4	23.91±2.096	19.15±1.66	20.74±0.50	15.15±0.69
5	40.18±3.899	32.05±1.14	30.89±1.25	20.62±1.17
6	68.44±6.314	41.84±6.22	39.37±1.30	29.03±1.92
7	95.57±3.57	61.47±3.18	53.82±3.01	31.53±1.90
8	99.74±0.338	77.06±7.98	62.03±1.91	35.51±2.49
9		82.14±2.55	71.15±3.72	43.95±2.49
10		94.05±4.85	78.59±6.45	54.12±0.87
11		99.91±0.095	86.76±2.15	59.79±1.07
12			91.99±0.52	73.22±1.31

All values are expressed is mean ± SD, n=3

Table 8:The in-vitro dissolution data of matrix tablets for formulations F5-F8

Time(Hr)	Formulations(% Cumulative drug release)			
	F5	F6	F7	F8
1	0.61±0.063	0.40±0.25	0.66±0.50	0.86±0.60
2	3.33±0.27	1.91±0.19	2.51±0.31	2.97±0.60
3	11.57±0.58	9.46±0.11	6.57±0.92	6.69±0.24
4	17.72±1.62	13.88±0.59	10.32±0.28	9.69±0.29
5	22.89±1.35	18.36±0.80	13.93±0.28	12.69±0.91
6	27.36±0.29	22.56±0.54	17.01±1.03	16.09±0.64
7	29.20±0.24	27.05±1.45	21.51±2.07	19.30±0.52
8	29.97±0.12	27.85±0.62	23.59±0.23	22.51±0.84

9	34.27±0.12	28.59±0.45	28.24±0.04	28.23±0.15
10	39.55±0.31	31.42±0.17	31.70±0.27	29.21±0.27
11	45.05±0.87	34.01±1.05	33.97±1.03	30.64±1.02
12	51.27±1.02	40.43±5.49	37.28±0.22	32.20±0.68

All values are expressed is mean ± SD, n=3

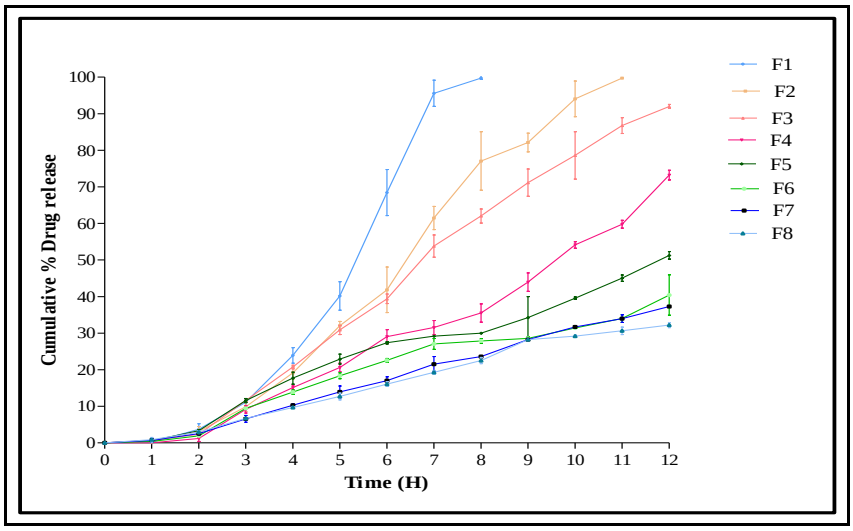

Figure 01: The dissolution profile of matrix tablets (F1-F8) of Diclofenac sodium

Figure 01 shows the drug release pattern of formulations F1-F8 which contain the polymer DRSG in the concentration range of 5% to 40%. As the drug had a half life of 2-2.5 hrs, for its once daily formulation, the sustain release was desired for at least for 12 hrs. It was observed that the formulations with DRSG showed a much more sustain release. Total amount of drug release from the formulation F3 & F4 upto 10hrs ranged between 50-70%. Other formulations, F1 & F2 indicating complete drug release within 10 hrs at low concentrations of DRSG and F5-F8 indicating incomplete drug release at high concentrations of DRSG. This may be due to the viscosity of polymer present in tablet increases with increase in the hydrogel (DRSG) concentration thus limiting the release of active ingredient. Also with fact that further increase in polymer amount, thicker gel forms inhibiting dissolution medium penetration strongly resulting in significant reduction in release value [11,13,14] On the other side, the formulation F3 formulation showed approximate 90% release in 12 hrs. Also formulations, F4 & F5 showed the drug release approximate 73 and 52%, with 20 and 25 % concentration of polymer respectively. This was selected for further study.

Effect of channeling agent on the release rate

The effect of channeling agent (PEG 4000) (C1, C2 and C3 respectively) was studied on the selected formulation. The in-vitro dissolution results and the drug release profile of these formulations are given below in table 10 and figure 03 gives the drug release profiles.

Table 10: The in-vitro dissolution data of matrix tablets for formulations C1-C3

Time(Hr)	**Formulations(% Cumulative drug release)**		
	C1	**C2**	**C3**
1	0.70±0.48	0.55 ±0.023	0.70±0.06
2	2.35±0.14	2.63±0.42	2.70±0.22
3	11.59±0.40	11.97±1.89	13.37±0.21
4	20.74±0.50	21.94±0.40	24.75±0.08
5	30.89±1.25	29.11±1.31	33.07±0.52
6	39.37±1.30	35.45±2.43	47.49±1.11
7	53.82±3.01	49.69±2.93	61.96±0.82
8	62.03±1.91	58.18±1.52	71.16±0.93

9	71.15±3.72	72.14±2.63	80.10±1.14
10	78.59±6.45	81.09±1.72	90.91±2.81
11	86.76±2.15	89.75±1.22	99.40±0.45
12	91.99±0.52	97.40±0.98	97.89±0.56

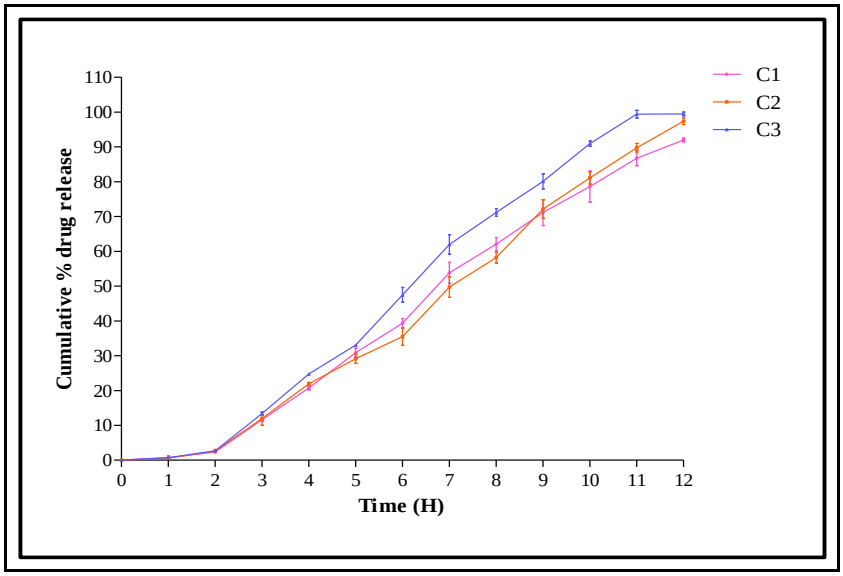

Figure 03: Drug release profile of C_1-C_3 formulations.

The PEG 4000 was used as channeling agent for the formulations. The result showed that there is significant increase in the drug release. As the amount of PEG 4000 (channeling agent) increased in the formulation % cumulative release of the drug increased. From this we can conclude that DRSG is the release controlling agent and PEG 4000 is the release improving (channeling) agent. The 3% and 5% concentration of PEG 4000 was selected for the furthered optimization.

Conclusion:

From the analysis of dissolution profile of preliminary trial formulations of tablets, it was found that, 15–25 % concentration of DelonixRegiaSeed Gum showed good drug release. Combination of various channeling agents like PEG was used for modulating the release profile. It was found that 3-5% concentration of PEG showed desirable change of drug release. The above concentration of DRSG and PEG was selected for optimization using Factorial design.Optimization studies with 3^2 full factorial designs were carried out using DRSG (X_1) and PEG (X2) as variable factors and by keeping both constant which were selected based on preliminary trials. From the mathematical models generated, an optimal formulation comprising of DRSG (17.63%) and PEG 4000 (3.80 %) was identified to provide desired values for percentage drug released at a 12 hr (90.19%) and the time required for a given percentage of drug to be released ($t_{50\%}$)(7.4 h).Both the factors were found to significantly affect the drug release from the matrix tablets. Optimized formulation exhibited sustained drug release with zero-order release kinetics and showed the case II drug release or anomalous drug release, indicating that two or more mechanisms for drug release are involved, that is, diffusion, erosion, and chain relaxation

References:

1. Ravi PR, Ganga S, Saha RN: Design and study of Lamivudine oral controlled release tablets. AAPS PharmSciTech 2007; 8(4): 1-9.
2. 2.Brahmankar DM, Jaiswal SB: Biopharmaceutics and Pharmacokinetics, A treatise. VallabhPrakashan, First Edition 2005.
3. Remington: The science and practice of pharmacy. LippincottWiliams and Wilkins, Twenty one Edition 2005.

4. 4.Ranade VV, Hollinger MA.Role of polymers in drug delivery. In: Drug delivery systems. 2nd edition.Florida, CRC Press, (2004) 64.
5. 5.Bharadwaj TR, Kanwar M, Lal R, Gupta A. Natural Gums and Modified Natural Gums as Sustained-Release Carriers. Drug Dev. Ind. Pharm.(2000) 26, 1025-1038.
6. Jackson RobertII L, Marrow JD. Analgesic- Antipyretic & anti-inflammatory agent and drug employed in the treatment of gout. In: Hardman JG, Limbird LE (Eds). Goodman and Gilman's The pharmacological basis of therapeutics. 10th edition.Mc-Graw Hill(2001).709-710.
7. 7.Katzung BG. Basic and clinical pharmacology. 8th edn.Lange Medical books/Mc-Graw Hill.Medical publishing division.2001: 604.
8. Sweetman SC (Ed) Martindale: The complete drug reference. 35th edition. London. The Pharmaceutical Press, (2007) 38-40.
9. Sreenivasa Reddy N, Mahendra Kumar C ,Rohith G, Chandrashekhar M . Sindhuabraham. Development of floating matrix tablets: an approach using natural gums.Ijpwr (2010) vol. issue 3 (Jun-Sep)
10. Anonymous, The Wealth of India, A Dictionary of Indian Raw Material and Industrial Product,vol. 3, CSIR, New Delhi.
11. Avinash R. Tekade, and Surendra G. Gattani. Development and evaluation of pulsatile drug delivery system using novel polymer.Pharmaceutical Development and Technology, 2009; 14(4): 380–387
12. Al-Saidan SM, Krishnaiah YSR, Patro SS, Satyanaryana V. In vitro and In Vivo Evaluation of Guar Gum Matrix Tablets for Oral Controlled Release of Water-soluble Diltiazem Hydrochloride.AAPS PharmSciTech.(2005) 6 (1), Article 5, E14-E21.
13. Hui H, Robinson JR, Lee VHL. Design and fabrication of oral controlled release drug delivery system. In: Robinson JR, Lee VHL (Eds), Controlled Drug Delivery: Fundamentals And Applications. 2nd edition.New York, Marcel Dekker, Inc.,(1978) 373.
14. Tommasina C, Pietro M, Carlotta M, Franco A. Polysaccharide hydrogels for modified release formulations. J. Control. Release, (2007).119, 5–24.

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