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STUDY OF POTENTIAL OF A NATURAL POLYMER AS A FORMULATION COMPONENT FOR THE DEVELOPMENT OF SUSTAINED RELEASE MATRIX TABLET

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ABSTRACT

Plant products serve as an alternative to synthetic products because of their local accessibility, eco friendly nature and cost effectiveness. An attempt was made to formulate sustained release matrix tablet using Oryza sativa hull. Preformulation studies comprising of characterization of Oryza sativa hull ascertained certain significant properties which proved helpful during the process of formulation development. The drug-excipient compatibility study by IR spectroscopy and DSC confirmed the absence of any interactions between the drug and the excipient. Matrix tablets were prepared using oryza sativa as a matrix forming polymer in different proportions. The method of preparation of matrix system and the concentration of the components had significant effect on the release of diclofenac sodium. The matrix tablets were evaluated for thickness, hardness, friability, weight variation, drug content and in-vitro drug release studies. The results suggest that Oryza sativa prolonged the release of drug through the matrix tablet. Oryza sativa thus promises considerable utility in the development of oral sustained release formulation.

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INTRODUCTION

Natural materials have advantages over synthetic materials because they are non toxic, less expensive and freely available. Furthermore, they can be modified to obtain tailor made materials for drug delivery systems allowing them to compete with the synthetic products that are commercially available. Many kinds of natural gums and mucilage are used in the food industry and are regarded as safe for human consumption. It should be noted that many 'old' materials are still popular today after almost a century of efforts to replace them. It is usual to strike a balance between economics and performance in the face of commercial realities. [1]

Oral extended release systems continue to dominate the market despite the advancements made in other drug delivery systems in order to increase the clinical efficacy and patient compliance. Oral extended release systems are mainly grouped into three types, e.g. reservoir, monolithic and matrix types.[2, 3] Among these hydrophilic matrix tablets are preferred in the formulations since most display good compression characteristics, even when directly compressed and have adequate swelling properties that lead to a rapid formation of external layer, allowing drug release modification.The release of drug from these systems is controlled by penetration of water through it produced by hydration of polymer and diffusion of drug through the swollen, hydrated matrix, in addition to the erosion of layer. The extent to which the erosion or diffusion controls the release depends on polymer selection as well as on the drug-polymer ratio used in the formulation. High drug polymer ratios result in formulations from which drug release is controlled by attrition.

Various natural gums and mucilages have been examined as polymers for sustained drug release, in the last few decades.[4, 5] The physical properties and the drug release mechanisms of the extended release preparations determine their *in-vivo* performance. The use of natural polymers and their semi-synthetic derivatives in drug delivery continues to be an area of active research despite the advent of synthetic polymers. Natural polymers remain attractive primarily because they are inexpensive, readily available, capable of multitude of chemical modifications and potentially degradable and compatible due to their origin.

Diclofenac sodium is used as an analgesic, antipyretic, anti-inflammatory and is approved in the United States for the long term symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Pharmacokinetic profile of Diclofenac sodium suggests that after oral administration, it is rapidly and almost completely absorbed. Its absorption is delayed by food. It is highly protein bound. Diclofenac undergoes first-pass metabolism, with 60% of unchanged drug reaching systemic circulation.[6] About 40% to 60% is excreted in the urine; the balance is excreted in the bile. Oral form of diclofenac sodium is contraindicated in the patients having hypersensitivity, hepaticporphyria, history of asthma, utricaria, late pregnancy, breast feeding and cautious in case of peptic ulcer.[7] Diclofenac sodium has many side effects like anxiety, depression, dizziness, edema, taste disorder, transient stinging, abdominal pain or cramps, bleeding, colitis.[8] The present invastigation is aimed to formulate the extended release tablet of diclofenac sodium with the aid of *Oryza sativa* hull.

MATERIALS AND METHODS:

The drug Diclofenac sodium was generously supplied as a gift sample by NuLife Pharmaceuticals, Pune-411018. *Oryza sativa* hull was purchased from the local market.

Development of excipient from Oryza sativa hull

Oryza sativa hull was blended in a blender to get fine powder. The powder mass was passed through 80# sieve and used for further studies.

Preformulation studies

Determination of calibration curve for Diclofenac Sodium: The λ_{max} of the drug was determined by scanning between 400 to 200 nm using a UV-visible spectrophotometer.[10]

Physicochemical characterization of *Oryza sativa* hull

Solubility of Oryza sativa hull powder was determined in different solvents.[9] The bulk density, tapped density, compressibility index and Hausners ratio were determined. Angle of repose is used to characterize the flow property of a powder material. It was determined by fixed height funnel method. Additionally physico-chemical properties like ash value, acid-insoluble ash value, loss on drying and viscosity were determined.

Compatibility Studies

The compatibility of Diclofenac sodium and *Oryza sativa* hull powder was studied using their multiple physical mixtures in ratio 1:1. The mixtures were prepared by triturating the drug with the powder and the mixtures were sealed in clear glass vials with LDPE stoppers, which were then charged into

stability chambers for 10 days at 40°C±2°C/75%±5% RH. The mixtures were used to study compatibility by DSC, FTIR and Assay.[11]

Preparation and evaluation of Diclofenac sodium matrix tablet:

Matrix tablet of Diclofenac sodium was prepared using different ratios of *Oryza sativa* hull powder as a matrix polymer.

Formulation of Diclofenac sodium matrix tablet: [12]

The tablet formulations were prepared by wet granulation technique as per table no.1. In the present formulation, Diclofenac sodium was the active pharmaceutical ingredient, *Oryza sativa* hull powder was tried as a matrix polymer, anhydrous lactose was added as a diluent, talc and magnesium stearate were included as glidant and lubricant respectively. All the ingredients were passed through ASTM-80# sieves. Required quantities of Diclofenac sodium, *Oryza Sativa* hull powder and Lactose anhydrous were mixed thoroughly in a mortar with the aid of a pestle to get the uniform mix and a sufficient volume of the granulating agent - water was added by spraying technique. After enough cohesiveness was obtained, the mass was sieved through ASTM-10# to get granules. The granules so obtained were dried and then were passed through ASTM-22#. Talc and magnesium stearate were added finally. The blends were subjected to evaluation. The formulation blends were then compressed as tablet using Karnavati minipress.D-II. The batches prepared were coded as F_1, F_2, F_3, F_4 and F_5. Following table represents the batchwise compositions of diclofenac sodium matrix tablets. All the quantities mentioned are in milligrams.

Table No. 1: Compositions of tablet batches

Ingredients	F_1	F_2	F_3	F_4	F_5
Diclofenac sodium	100	100	100	100	100
Oryza sativa hull powder	50	75	100	125	150
Lactose anhydrous	140	115	90	65	40
Distilled water	q.s	q.s	q.s	q.s	q.s
Talc	5	5	5	5	5
Magnesium stearate	5	5	5	5	5

Evaluation of tablets:

The formulation blends were evaluated for micromeritic properties.After formulation, the tablets were evaluated for tests viz.Thickness, [13] Hardness, [14] Uniformity of Weight [15] and Friability. [16]

***In-Vitro* Drug Release from Tablets: [17]**

Additionally the formulations F1, F2, F3, F4 and F5 along with a similar marketed formulation, were subjected to *in-vitro* drug release study. The drug release studies were performed by USP Type II dissolution test apparatus. 7.5 pH phosphate buffer was used as a dissolution medium. The absorbance values were measured at 276nm for Diclofenac sodium by U.V-Visible spectrophotometer. The readings were taken in triplicate.

RESULTS AND DISCUSSION:

The scanning of Diclofenac sodium solution in the UV range showed maximum absorbance at 276 nm which confirmed its purity and hence, the calibration curve was determined at this wavelength. The values are given in Figure No.1.

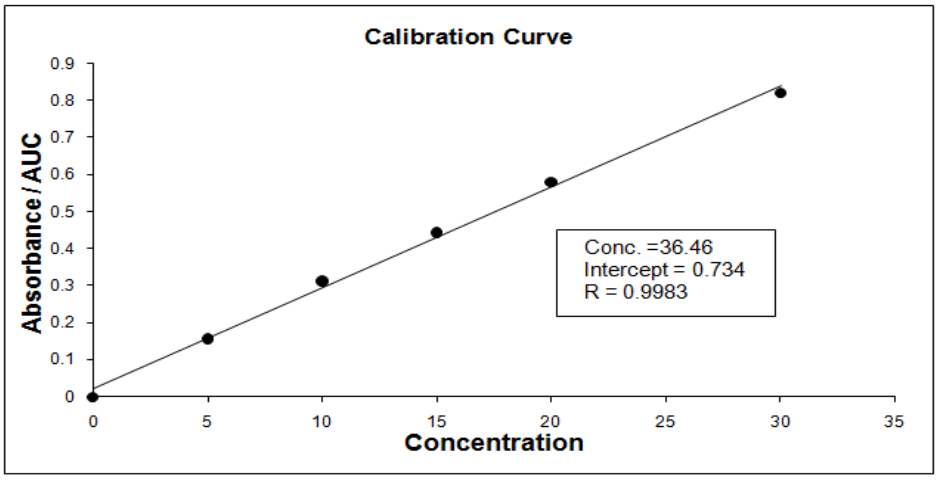

Figure No.1: Calibration curve for Diclofenac sodium

Physicochemical characterization of *Oryza sativa* hull powder: The natural excipient was subjected to evaluation of various physicochemical properties. They are shown in Table No.2.

Table No.2: Physicochemical properties of *Oryza sativa* hull powder

Sr. No	Parameters	Results
1.	Bulk density	0.547(g/cm^3)
2.	Tap density	0.657(g/cm^3)
3	Compressibility index	18.17%
4.	Hausner's ratio	1.206
5.	Angle of repose	33.07^o
6	Ash value (%)	10
7	Acid-insoluble ash value (%)	4
8	Loss on drying (%)	5.10
9	Viscosity (mPa.s)	14.57

Scanning Electron Micrograph:

The scanning electron micrograph of *Oryza sativa* hull powder particles at magnification of 1000x and 2000x are as shown in Figure No.2

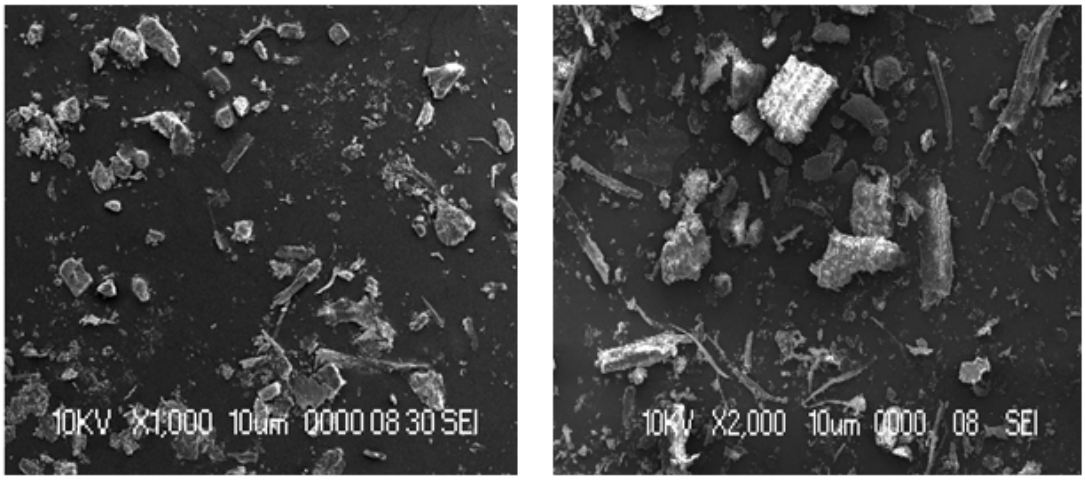

Figure No. 2: Scanning electron micrographs of *Oryza sativa* hull powder

Compatibility Studies:

FTIR spectroscopy, DSC technique and Assay method were followed to check the drug – excipient compatibility.

FTIR Study: The compatibility between the drug and the selected polymers was evaluated using FTIR peak matching method. Figure No. 2 depicts the concerned FTIR peaks.

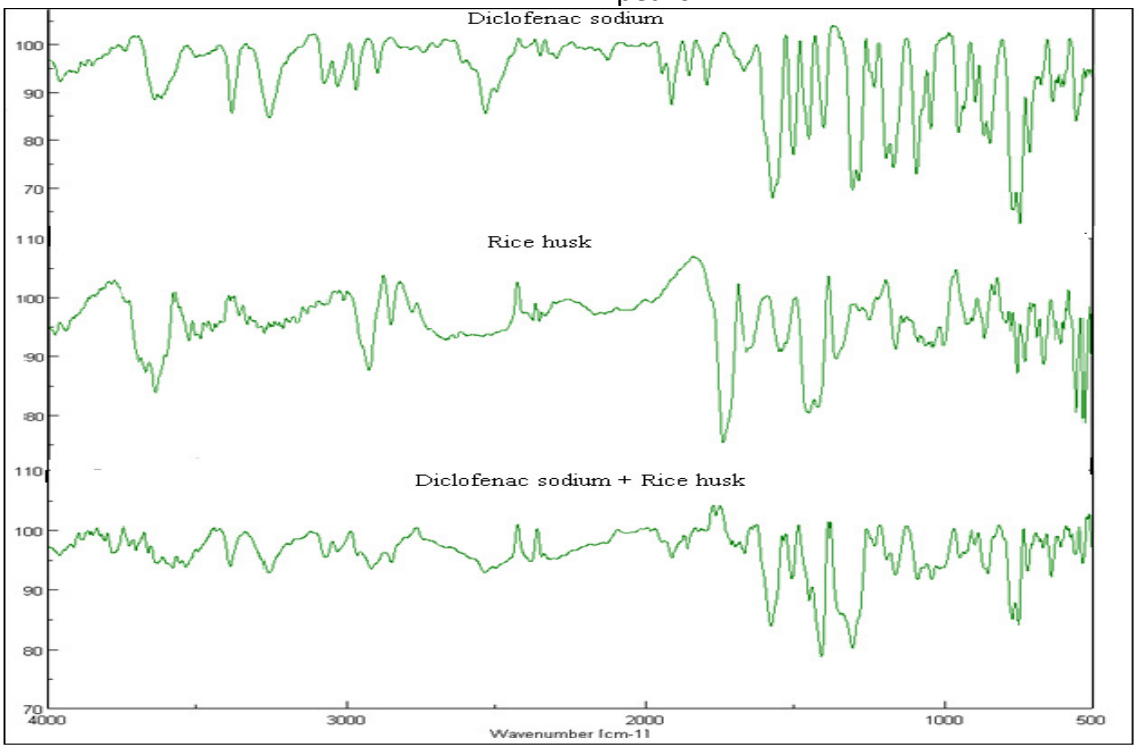

Figure No.2: Compatibility study using FTIR spectroscopy

There was no appearance or disappearance of peaks in the polymer-drug mixture, which confirmed the absence of any chemical interaction between the drug and the polymer.

DSC styudy: It is depicted in Fig. No. 3.

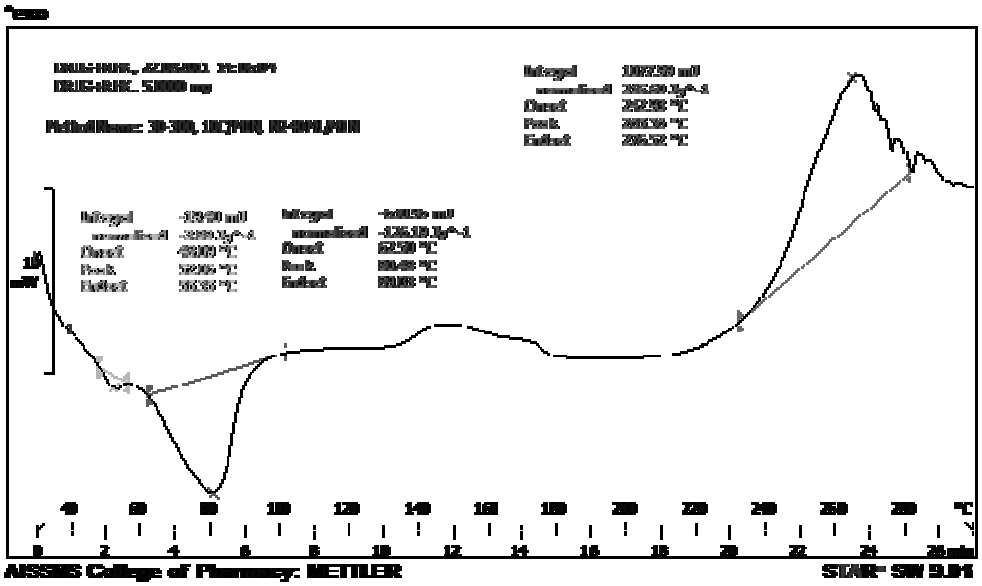

Figure No.3: Compatibility styudy using DSC

The drug Diclofenac Sodium showed a sharp melting endotherm at 280^{0}C and exothermic at 85^{0}C. *Oryza sativa* hull (Rice husk) powder showed a broad melting endotherm at 59^{0}C which indicates no interaction between drug and *Oryza sativa* hull powder.

Assay method: The drug showed 98.89 % purity. This in turn confirms less or non significant interaction between the drug and the excipient.

Evaluation of formulation blends:

The formulation blends were evaluated for micromeritic properties.

Table No.3: Micromeritic properties of formulation blends

Parameters	F1	F2	F3	F4	F5
Bulk density (gm/ml)	0.45	0.35	0.50	0.52	0.55
Tapped density (gm/ml)	0.49	0.39	0.55	0.60	0.69
Hausner's ratio	1.08	1.114	1.09	1.53	1.181
Compressibility index(%)	8.16	10.25	9.08	13.33	15.37
Angle of repose	23.89^0	23.59	24.61	25.43	27.44

The above data of micromeretics properties of the blends was acceptable and within the limit.

Evaluation of Tablets: Table No.4 contains the data of evaluation of tablets for various parameters.

Table No.4: Evaluation of Tablets

Sr. No	Parameters	F1	F2	F3	F4	F5
1	Thickness(mm)	2.78	2.71	2.65	2.62	2.65
2	Hardness(kg/cm^2)	4.46	4.23	4.53	4.43	4.33
3	Weight Uniformity(mg)	0.52	0.56	0.51	0.53	0.56
4	Friability (%)	0.30	0.15	0.14	0.13	0.12

In-Vitro Drug Release from Diclofenac sodium Matrix Tablets: Table No.5 depicts the drug release profile for various formulations.

Table No.5: % Drug release for formulations

Time in Hours	% Drug Release					
	F_1	F_2	F_3	F_4	F_5	Marketed
1	32.5	26.24	21.58	21.31	22.24	27.34
2	45.96	35.26	32.69	30.14	31.95	32.38
3	56.29	43.21	40.86	35.12	36.5	46.26
4	60.26	49.36	48.09	44.31	38.53	61.62
5	72.67	58.64	56.01	52.64	43.71	69.71
6	79.61	67.31	64.23	59.31	49.29	76.71
7	85.38	74.81	71.82	67.34	52.21	83.27
8	92.83	81.64	79.23	76.21	58.78	93.83

9	98.7	88.64	84.26	82.12	67.5	98.31
10	--	95.64	89.21	88.94	72.21	--
11	--	100.1	95.2	94.21	78.64	--
12	--	--	101.06	99.31	85.74	--
13	--	--	--	--	93.36	--
14	--	--	--	--	99.34	--

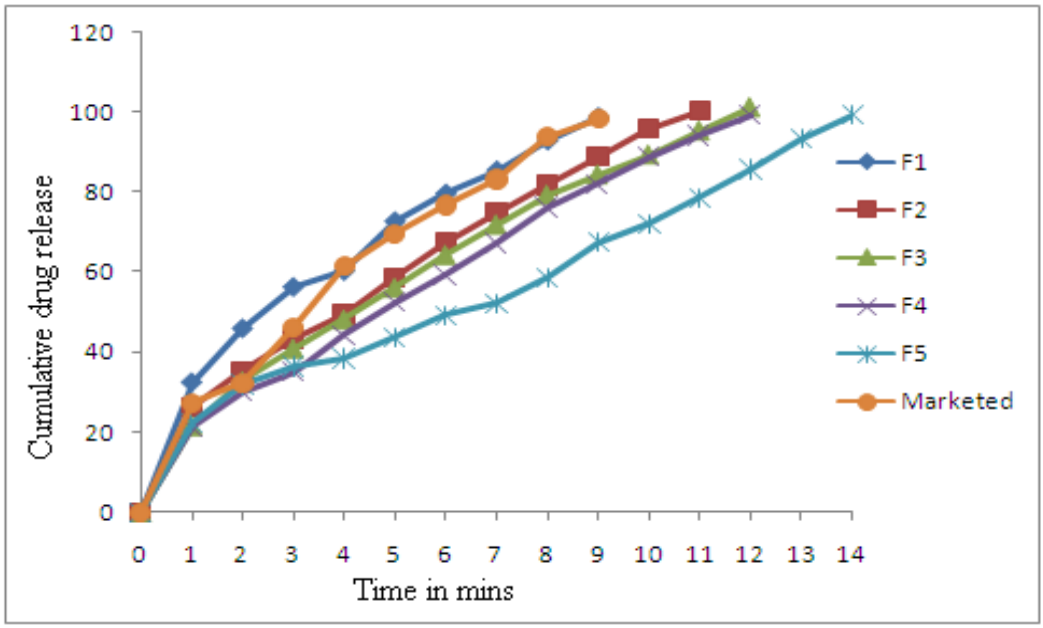

Figure No.4: Drug release profile for formulations

Selection of optimized batch:

The prepared tablet batches were compared with the marketed tablet for release characteristics. All the batches of the the prepared matrix tablets of Diclofenac sodium meet the requirement as per USP which is 85% drug release in 16 hours. It is evident from the % drug release data and the drug release profile of the formulations that all the batches showed promising results. The cumulative % drug release was found to be 98 % in 9 hours for the marketed formulation while in case of the formulation batch F_5 it was 99.34 % in 14 hours. This explains the competency of formulation batch F5.Hence it was considered as the optimized batch.

CONCLUSION:

Matrix tablets were prepared by wet granulation method using *oryza sativa* as a matrix forming material in different proportions. Preformulation Studies comprising of characterization of Oryza sativa hull ascertained certain significant properties which proved helpful during the process of formulation development. The drug-excipient compatibility study by IR spectroscopy and DSC confirmed the absence of any interactions between the drug and Oryza sativa hull powder. The prepared formulations were subjected to performance evaluation.

Comparative evaluation of the matrix tablet with the marketed sustained release formulation explained their competent dissolution profiles. The comparative *in-vitro* drug release of the batches F1 to F5 was considered for the selection of optimized batch. The batch F5 possessed the highest potential to release the drug gradually for more than 14 hrs.

It confirmed the fact that the formulated tablet showed promising results to be a sustained release formulation. It is evident from the overall studies that, *Oryza sativa* hull possesses potential for sustained release of the drug from the tablet.

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