PHARMACEUTICAL AND BIOLOGICAL EVALUATIONS
April 2016; vol. 3 (Issue 2): 241-255.
www.onlinepbe.com
ISSN 2394-0859

Research Article

Formulation and evaluation of tamarind seed polysaccharide matrix tablet

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Received: 11 March 2016
Revised: 28 March 2016
Accepted: 01 April 2016

ABSTRACT

Objective: The objective of using natural polymer was to modify the release rate of Diclofenac sodium from matrix tablet. The matrix forming agent like Tamarind seed Polysaccharide show sustained release property in tablet which is obtained naturally from fruit of *Tamarindus indica* L. belonging to Family Leguminosae.

Methods: The sustained release matrix tablet of Diclofenac sodium were prepared by wet granulation technique using varying concentration of hydrophilic polymer i.e. TSP.

Results: OF1 and OF2 both are optimized batch. The *in vitro* dissolution study was carried out for optimized as well as marketed formulation (Voveran- SR). Both the optimized batchesat 10 h were found to be 90.27% and 90.18%, respectively.

Conclusions: Tamarind seed polysaccharide can be employed in dosage form to sustain the drug release. Tablet formulated with various concentrations of Tamarind seed polysaccharide (TSP) gives release up to 10 h and more. OF1 and OF2 both formulations give comparable release with marketed formulation. From the present work it can be conclude that, the objectives which were set at the beginning of the study got fulfilled.

Keywords: Diclofenac sodium, Tamarid seed polysaccharide, Matrix forming agent

Introduction

Tamarind is amongst most common and commercially important large evergreen tree that is grown abundantly in the dry tracks of Central and South Indian states, and also in other South East Asian countries. Following parts of fruit of *Tamarindus indica* L. belonging to the family Leguminosae are commercially very important: Pulpy portion of the fruit mainly used as acidulate in Indian recipes. Tamarind gum is obtained from the kernel of the seeds powder. Tamarind products are widely used in Asia and also used in some part of Africa. In Asian countries, especially India, tamarind is mainly cultivated and used as a gelling, and acidifying agent. Tamarind gum along with *xanthan gum*, hydroxypropyl cellulose is used for nasal

mucoadhesion studies in powder formulation. Tamarind gum is also used for as a bioadhesive tablet.[1,16,20,23,24,27]

Matrix tablets composed of drug and polymer as release retarding material offer the simplest approach in development a sustained release system. For sustained release systems, the oral route of drug administration has received the most interest as it is natural, uncomplicated, convenient and safer route. Matrix tablets were prepared by direct compression method. Mucilages are composed of heterogenous polysaccharide complexes formed fromthe sugars, arabinose, galactose, glucose, mannose, xylose and uronic acid units. Mucilages possess a variety of pharmaceutical properties, which make them useful as additives in pharmaceutical preparations and in present investigations, mucilages plays important role in design of formulations.[2-7,14,21,23]

Materials and Methods

Materials

Diclofenac Sodium, Tamarind Seed Polysaccharide

Method of extraction of tamarind gum

Method 1

200 g of tamarind seeds was soaked in double distilled water and boiled for 5 hr to remove the outer dark layer. Often the outer dark layer is removed, to the inner white portion sufficient amount of double distilled water was added and boiled with constant stirring to prepare the slurry. Now cool the resultant solution in refrigerator so that most of the undisclosed portion settles down. The supernatant liquid can be separated out by simple decantation or best by centrifugation at 500 rpm for 20 min. After this, the solution is concentrated on a water bath at 60°C to reduce the volume to one-third of the initial volume. Now cool the solution and pour into 3 volumes of acetone by continuous stirring. Precipitates obtained were washed with acetone and drying in vacuum at 50-60°C.[1,8,9,11-13,15]

Method 2

Tamarind seeds were collected and dried in sunlight. The kernels are than crushed to fine powder. 20 g of fine kernel powder was added to 200 ml of cold distilled water to prepare slurry. The slurry obtained is than poured into 800 ml of boiling distilled water and are boiled for 20 min on a water bath; a clear solution was obtained which was kept overnight. The thin clear solution was than centrifuged at 5000 rpm for 20 min to separate all the foreign matter. Supernatant liquid was separated and poured into excess of absolute alcohol with continuous stirring. Precipitates were obtained which were collected by a suitable method and washed with 200 ml of absolute ethanol and dried at 50°C for 10 hr. Store the polymer obtained in desiccators.[17-19, 24-26]

Method 3

This method is patented in United States by Jones et al. It involves the separation of tamarind kernel powder on the basis of their size distribution. Tamarind kernel powder was defatted by using C-6 or C-8 aromatic hydrocarbons or C-1 or C-2 or above halogenated lower hydrocarbons or C-1 or C-5 mono or dihydroxy alcohols, e.g. ethylene dichloride, heptanes, or toluene. (For defatting Crude TKSP is suspended in suitable solvent to extract fat that is mechanically recovered by filtration or centrifugation and dried.) After drying, HiSil or other silicaceous materials like CabOSil improve the flow properties of powder. The powder is further grounded by using Hammer mill or Pin mill that will reduce the size of the powder below 100 mm. The powder is further air classified by using suitable air classifier. Three fractions of the powder were obtained after air classifications: 10-20% of fine fraction rich in protein.60-80% of moderately fine fraction rich in polysaccharides.10-20% of the coarser fraction rich in mechanical properties. TSP can be isolated from the moderately fine powder fraction of the powder obtained after air classification.[10,22,28,29,30]

Results and Discussion

1) Characterization of Diclofenac sodium

a) *Melting point of Diclofenac sodium:* The melting point was found to be in the range of 280 to 282^{0}c.

b) *Spectroscopic studies*

UV spectroscopy: (Determination of λ max.)

The UV spectrum obtained is shown in Figure 1. The wavelength of maximum absorbance (λ max) was found to be 276 nm in Methanol (A.R. grade) and Phosphate buffer pH 6.8.

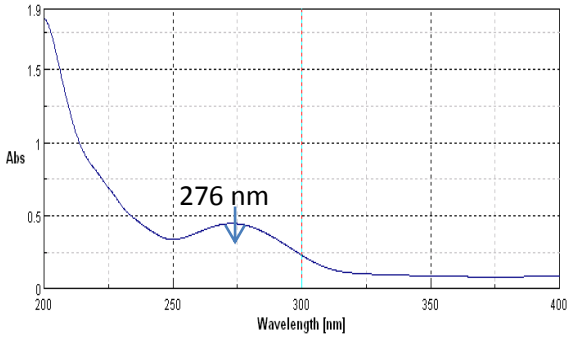

Figure 1: UV spectra of Diclofenac sodium.

Preparation of standard curve (calibration curve) of Diclofenac Na in Phosphate Buffer (pH 6.8)

Table 1: Data of concentration and absorbance.

Sr. No.	Concentration (µg/ml)	Absorbance at 276 nm
1	2	0.1012
2	4	0.1891
3	6	0.2492
4	8	0.3219
5	10	0.3991
6	12	0.4849
7	14	0.5972

The graph of absorbance versus concentration for pure Diclofenac sodium is shown in Figure 2. It was found to be linear in the concentration range of 2-14 µg/ml at 276 nm. Hence the drug obeys the Beer's- Lambert law in this range.

Table 2: Data for standard curve parameters.

Sr. No.	Parameters	Values
1	Correlation coefficient (R)	0. 922
2	Slope	0.039
3	Intercept	0.016

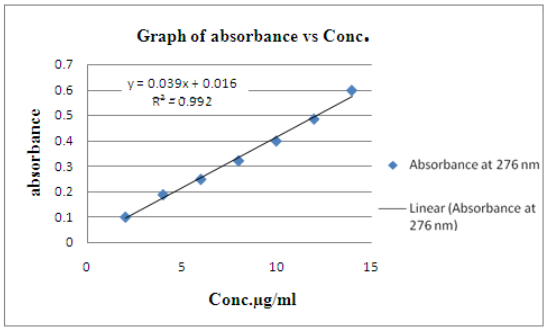

Figure 2: Calibration curve of Diclofenac sodium in phosphate buffer (pH 6.8).

Preparation of standard curve (calibration curve) of Diclofenac Na In 0.1 N HCl.

Table 3: Data of concentration and absorbance.

Sr. No.	Concentration (µg/ml)	Absorbance at 276 nm
1	2	0.0993
2	4	0.1338
3	6	0.1721
4	8	0.1935
5	10	0.229

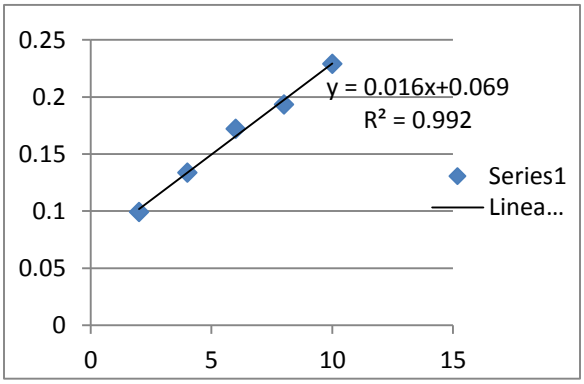

Figure 3: Calibration curve of Diclofenac Na in 0.1 N. HCl (absorbance vs concentration).

IR spectrum interpretation

Infrared spectrum of Diclofenac sodium was recorded. The observed peaks are match with the peaks given in pharmacopoeia which confirms that the supplied samples was of Diclofenac sodium.

Table 4: Data for standard curve parameters.

Sr. No.	Parameters	Values
1	Correlation coefficient (R)	0. 992
2	Slope	0.016
3	Intercept	0.069

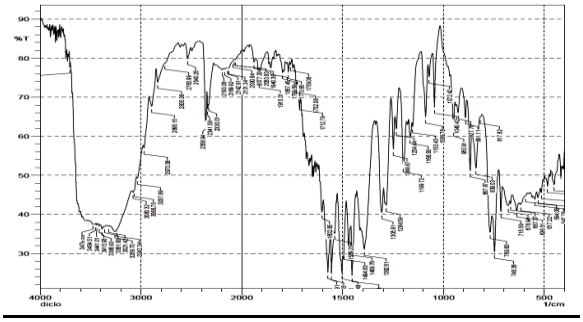

Figure 4: FTIR spectrum of Diclofenac sodium.

Table 5: IR spectrum interpretation of Diclofenac sodium.

Sr. No.	Frequency (cm^{-1})	Assignment
1	3454.54 cm^{-1}	N-H stretching
2	1591cm^{-1}	N-H bending
3	748.38cm^{-1}	C-Cl Stretching
4	1153.57cm^{-1}	Ar-H Bending
5	778.9,715.59,667.37cm^{-1}	Disubstituted chlorine
6	1539.20cm^{-1}	CH_2 Deformation
7	1712.79,1759.08 cm^{-1}	C=O Stretching

2) Tests for Tamarind seed polysaccharide

a) Preliminary test for Tamarind seed polysaccharide

Table 6: Identification test for TSP.

Sr. No.	Test	Result
1	Swelling by ethanol solution	Negative
2	Colour reaction with conc HCl	Yellow
3	Colour reaction with 5N NaOH	Yellow

Identification test for tamarind seed polysaccharide was performed as per article as all result found to be positive from above result it confirmed that powder obtained shows gum property .

b) Determination of purity of polysaccharide (+ Present; - Absent)

Table shows determination of purity of polysa ccharide by using various tests. Result obtained shows that polysaccharide which was extracted is pure as result obtained are negative only carbohydrates test are positive.

Table 7: Test for purity of gum.

Sr. No.	Tests	*T. indica*
1.	**Tests for steroids:** Salkowski test, Liebermann- burchard test	-ve
2.	**Tests for triterpenoids**: Salkowski test, Libermann-Burchard test	-ve
3.	**Tests for saponins**: Foam test, Haemolysis test	-ve
4.	**Tests for carbohydrates**: Molisch test, Barfoed's test Benedicts test	+ve
5.	**Tests for alkaloids**: Mayer's test, Hager's test, Dragendorff's test	-ve
6.	**Tests for flavonoids(after hydrolysis)** Shinoda test, Zinc/HCL reduction test	-ve

c) Confirmatory tests for extracted polysaccharide

Table 8: Confirmatory tests for extracted polysaccharide.

Sr. No.	Test	Observation	Inference
1.	**Molisch Test:** 2ml of sample solution (1%w/v) with 5 drops of Molisch's reagent in a test tube. Add gently through the side of test tube, about 2 ml of Conc. Sulphuric acid.	Violet ring at the junction of two liquids was seen	Carbohydrate present
2.	**Solubility:** Sample + Water	Sparingly soluble	Polysaccharide Present.
3.	**C.T. For glucose:** 2 ml of test solution+5%NaoH Solution	Brown precipitate was observed.	Glucose Confirm.
4.	**Foulger's Test:** 3 ml of Foulgers's reagent+1 ml test sol. Boil for 45 seconds and shake well. **Foulger's Reagent:** 40 g of urea in 80 ml of sulphuric acid (40% v/v) then add 2 g of stannous chloride boil until clear solution obtain.	Blue green color was developed	Galactose and xylose confirm

3) Physiochemical characterization of TSP

a) Physical Parameters

i) Organoleptic properties:

Yellowish cream colour of the polymer was observed.

b) Solubility:

Table 9: Solubility of TSP.

Sr. No.	Solvent	Solubility
1.	Water	Sparingly soluble
2.	Warm water	viscous colloidal solution
3.	Chloroform	Insoluble
4.	Ethanol (95%)	Insoluble
5.	Isopropyl alcohol	Insoluble
6.	Dichloromethane	Insoluble

c) Loss on Drying:

The loss on drying of TSP was found to be 6.78 %.

d) Angle of Repose:

The angle of repose of polymer was found to be 26.10 ± 0.13 which means powder has good flow property.

e) Density:

i) Bulk Density: Bulk density of powder was found to be 0.6410 ± 0.0069 g/ml

ii) Tapped Density: Tapped density of powder was found to be 0.7462 ± 0.0091 g/ml

f) Compressibility index:

Compressibility index of powder was found to be 14.07 ± 1.696 % which shows that powder has good flow property.

g) Hausner's ratio:

Hausner's ratio of powder was found to be 1.45 ± 0.058 which indicate that powder has good flow property.

h) Viscosity measurement:

The viscosity of 1 % (w/v) TSP solution was found to be 257.4 ± 0.01 cps.

i) *Melting point determination*

Melting point of TSP was measured and it was found that the material showed charring instead of melting in the range of 250 ºC - 260 ºC.

j) *Infrared spectroscopy*

Fourier transform infrared (FTIR) spectra of the samples were obtained in the range of 400 to 4000 cm-1 using a FTIR Spectrophotometer by the KBr disc method. The FTIR spectrum of TSP is shown in Figure 5.

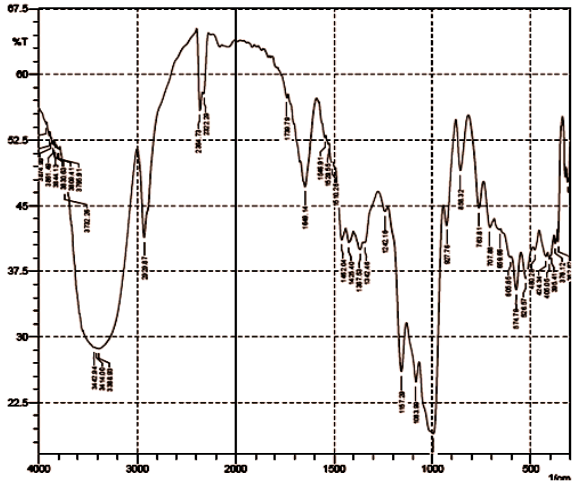

Figure 5: FTIR spectrum of TSP.

Interpretation

Table gives the interpretation of the peaks obtained in the IR spectra along with their corresponding functional groups. From the FTIR spectra it is observed that, the peaks at 1083.99 cm^{-1} indicates presence of C-O stretch, 3388.93 cm^{-1} O-H stretching,1083.99 cm^{-1} C-C stretching.

Table 10: IR spectrum interpretation of TSP.

Sr. No.	Frequency (cm^{-1})	Assignment
1.	3388.93 cm^{-1}	O-H stretch
2.	2929.87	C-H Stretch
3.	1649.14,1462.04	CH_2-Stretch
4.	1367.53,1242.16	OH-Plane bend
5.	1157.29	Glycosidic linkage
6.	1083.99	Coupled CO Stretch
7.	927.76	Ring Vibration

Drug - polymer compatibility study

The IR spectrum did not show presence of any additional peaks for new functional groups indicating no chemical interaction between diclofenac sodium and Tamarind seed polysaccharide.

FTIR spectrum of Diclofenac sodium and TSP

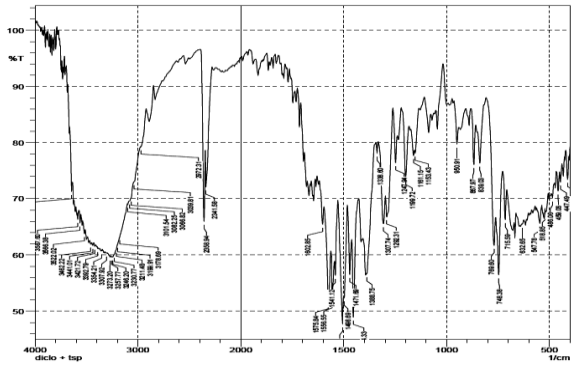

Figure 6: FTIR spectrum of Diclofenac sodium and TSP.

Evaluation of granules

Loose bulk density (LBD) and Tapped bulk density (TBD)

Bulk density depends upon particle size, shape, and tendency of particles to adhere together. The value for LBD and TBD has been shown in Table 11. These were found in the range of 0.516 ±0.007 g/ml to 0.5883±0.01 g/ml and 0.5605±0.005 g/ml to 0.6579±0.007 g/ml for granules respectively. Bulk densities of blends were found to be quite high which indicates that there is no excessive air voids and hence the granule mass do not pose any problem during compression. i.e. These values may further be correlate with compressibility index and tablet dissolution.

Angle of repose and compressibility index

The values of angle of repose have been shown in Table 11. The angle of repose and Compressibility Index of granules were found in the range of 25.98±0.3 to 28.26± 1.86 and 7.11±2.99 % to 12.66± 1.245 % respectively.

Table 11: Data for evaluation of granules.

Sr.No.	Formulations	Loose Bulk Density (LBD) (g/ml)	Tapped Bulk Density (TBD) (g/ml)	Compressibility Index (%)	Angle of Repose (θ)
1.	F1	0.5883± 0.01	0.627±0.003	9.447±1.77	27.96±0.06
2.	F2	0.5253±0.004	0.585±0.008	10.28±0.645	26.63±0.27
3.	F3	0.516±0.007	0.5733±0.005	10.003±0.386	26.49±0.63
4.	F4	0.533±0.007	0.593±0.006	10.16±0.302	28.26±1.86
5.	F5	0.520±0.018	0.5605±0.005	7.11±2.99	27.30±0.40
6.	F6	0.5374±0.009	0.5977±0.0089	10.06±1.72	27.34±0.45
7.	F7	0.5217±0.011	0.597±0.0087	12.66±1.245	27.05±0.40
8.	F8	0.5534±0.003	0.6196±0.003	10.67±0.899	25.98±0.3
9.	F9	0.5844±0.004	0.6579±0.007	11.15±0.471	26.49±0.4

All Values are expressed as mean ± SD, n=3.

Table 12: Physical evaluation data for the compressed tablets containing various concentrations of polymer.

Sr.No.	Formulations	Thickness (mm)	Weight Variation	Hardness (Kg/cm^2)	Friability (%)	Uniformity of Drug Content (%)
1.	F1	3.14 ± 0.03	348.86 ± 0.440	5.73 ± 0.249	0.260 ± 0.047	99.8 ± 0.60
2.	F2	3.35 ± 0.02	348.88 ± 0.510	5.53 ± 0.52	0.226 ± 0.055	99.3 ± 0.57
3.	F3	3.52 ± 0.01	348.43 ± 0.88	5.73 ± 0.24	0.22 ± 0.0326	98.7 ± 0.98
4.	F4	3.36 ± 0.04	348.45 ± 1.30	5.46 ± 0.24	0.37 ± 0.074	99.9 ± 0.65
5.	F5	3.65 ± 0.02	348.14 ± 0.855	5.46 ± 0.09	0.323 ± 0.032	99.1 ± 0.57
6.	F6	3.26 ± 0.08	348.56 ± 0.530	5.26 ± 0.09	0.43 ± 0.0801	99.1 ± 0.65
7.	F7	3.45 ± 0.05	346.91 ± 0.668	5.33 ± 0.09	0.29 ± 0.014	98.0 ± 0.98
8.	F8	3.67 ± 0.02	348.26 ± 0.736	4.93 ± 0.09	0.543 ± 0.112	98.2 ± 0.95
9.	F9	3.65 ± 0.06	348.43 ± 0.922	5.93 ± 0.09	0.363 ± 0.110	98.0 ± 0.98

All Values are expressed as mean ± SD, n=3.

Lubrication with magnesium stearate and talc improved the flow property.

6. Evaluation of tablets

The results are shown in Table 12.

7. *Physical parameters*

Thickness

Tablets has shown thickness values in the range of 3.14 ± 0.03 mm to 3.67 ± 0.02 mm.

Weight variation test

The pharmacopoeial limits for deviation for tablets of more than 250 mg are ± 5%. The average percentage deviation for all tablet formulations was found to be within the specified limits and hence all formulations complied with the test for weight variation.

Hardness and friability

The tablets showed hardness values ranging from 4.93 ± 0.09 to 5.93 ± 0.09 kg/cm^2, However these values alone cannot be considered as absolute indicator of their strength. Another measure of a tablet's strength is friability. Conventional compressed tablets that lose less than 1% of their weight are generally considered acceptable. In present study, the friability values for all the tablet

Table 13: Swelling Index of the tablet batches (F1-F9).

Sr. No	Swelling index (%)									
	Time (Hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	1	29.76	29.45	30.67	29.35	30.35	31.60	33.15	31.27	31.72
2	2	34.95	35.22	35.89	36.54	36.74	37.79	39.5	37.70	37.80
3	3	40.85	41.76	41.75	43.77	42.4	43.98	44.35	44.64	44.42
4	4	44.29	45.03	44.57	46.29	48.89	50.76	52.15	53.29	52.85
5	5	53.18	54.17	51.41	55.65	57.9	56.17	58.71	57.21	58.28
6	6	46.47	47.59	48.57	48.85	48.57	51.98	52.0	51.29	51.42
7	7	42.32	43.55	42.55	43.72	41.44	45.13	43.17	44.11	45.32
8	8	35.52	36.12	35.43	31.26	34.49	35.96	36.14	37.51	37.71
9	9	30.11	39.15	28.56	29.85	31.98	31.51	29.14	30.83	29.28
10	10	26.35	26.11	25.11	25.45	24.29	25.42	25.12	25.75	24.25

Table 14: The *in vitro* dissolution profile of diclofenac sodium containing tamarind seed polysaccharide matrix tablets (formulations F1 to F4) and marketed tablet.

Sr. No.	Cumulative Percent Drug Release (%)					
	Time (Hrs)	Marketed	F1	F2	F3	F4
1	1	0340±0.19	12.28±0.28	8.27±2.00	5.95±0.20	5.35±1.50
2	2	1.74±0.29	12.78±0.21	8.98±1.84	7.87±0.70	7.25±0.97
3	3	19.45±2.42	25.51±10.2	25.53±1.28	19.87±1.08	18.89±0.24
4	4	42.6±0.22	46.34±1.19	34.25±2.03	29.23±0.94	44.65±1.17
5	5	47.71±0.27	52.49±0.80	47.67±1.08	36.69±1.02	53.42±1.89
6	6	57.52±2.21	62.18±1.07	60.27±1.00	52.08±1.22	59.60±1.22
7	7	70.67±1.30	69.08±0.83	70.50±1.36	60.84±0.76	70.82±0.95
8	8	75.31±0.71	77.66±1.81	79.41±1.28	73.98±4.77	77.55±1.33
9	9	82.58±1.27	88.18±0.20	89.41±1.12	91.75±0.68	86.39±1.13
10	10	90.68±0.54	96.09±1.02	95.05±0.75	94.15±1.70	92.52±0.97

formulations were found to be <1%, indicating that the friability is within the prescribed limits.

Swelling index

From the above Table 13 and Figure 7 we conclude that the process of the drug release from tamarind seed polymer involves water penetration in to the matrix by hydration and swelling of the polymer. As the polymer concentration increases, swelling index was found to increases up to some duration of time and after that limit tablets exhibits its erosion and hence swelling index get decreased. The swelling behavior indicated the rate at which this formulation absorbed water from dissolution

media and swelled. It has been observed that the cumulative present drug release decreases with increasing concentration of the polymer.

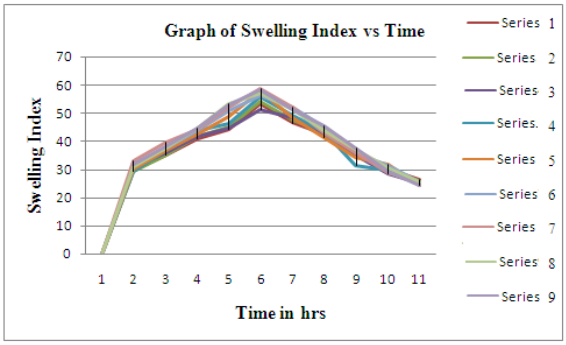

Figure 7: Swelling index of the tablet.

Chemical parameters

Uniformity of drug content

Uniformity in drug content was found within and among the different types of tablet formulations. The values ranged from 98.0±0.98 % to 99.9±0.65 % of labeled amount. Hence the tablet prepared passes the pharmacopoeial limit.

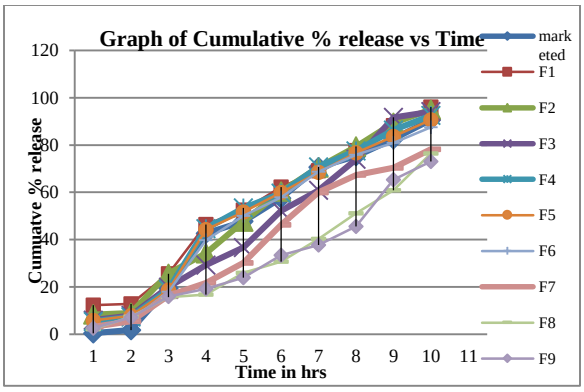

Figure 8: Dissolution profile of hydrophilic matrix tablets.

Dissolution test

The release profiles of Diclofenac sodium from the different formulations has been shown in Table 14 and Table 15. The data clearly indicate the drug release can effectively be sustained by varying the concentration of polymer. The batch F1, F2, F3….up to F9 showed the drug release more than 10 hrs. All the formulations showed very low drug release in 0.1 N HCl (pH 1.2). This was due to the very low solubility of

Table 15: The *in vitro* dissolution profile of diclofenac sodium containing tamarind seed polysaccharide matrix tablets (formulations F5 to F9).

Sr. No.	Cumulative Percent Drug Release (%)					
	Time (Hrs)	F5	F6	F7	F8	F9
1	1	5.70±1.34	3.16±2.94	3.13±2.67	2.04±0.86	2.44±1.04
2	2	7.74±0.25	5.92±0.88	5.45±2.43	7.42±0.44	7.17±0.50
3	3	18.61±0.33	17.97±0.51	16.20±0.99	15.69±0.06	15.90±0.09
4	4	44.27±1.76	39.69±4.47	21.67±5.07	16.78±0.70	19.11±0.13
5	5	51.67±1.37	50.05±2.22	30.14±1.43	25.92±0.89	23.85±0.51
6	6	59.90±1.46	57.89±1.18	46.24±4.61	30.73±1.25	33.45±0.92
7	7	68.49±0.86	68.72±0.53	59.98±2.37	40.29±0.93	37.77±0.82
8	8	76.68±1.97	75.86±2.77	67.37±1.84	51.13±1.58	45.58±1.65
9	9	83.60±2.76	80.95±1.70	70.42±0.28	60.88±1.24	65.32±0.36
10	10	90.63±2.21	87.57±1.88	78.24±1.47	76.47±1.15	73.12±0.99

Table 16: The dissolution models for matrix tablets (F1-F9) of Diclofenac sodium.

Sr. No.	Formulation code	R^2				
		Zero order	First order	Korsmeyer Peppas	Higuchi	Hixson-Crowell model
1.	F1	0.958	0.953	0.893	0.938	0.957
2.	F2	0.985	0.973	0.937	0.953	0.971
3.	F3	0.980	0.971	0.962	0.937	0.945
4.	F4	0.980	0.962	0.957	0.952	0.975
5.	F5	0.976	0.959	0.941	0.952	0.965
6.	F6	0.981	0.967	0.941	0.960	0.973
7.	F7	0.986	0.962	0.950	0.907	0.936
8.	F8	0.981	0.973	0.979	0.929	0.953
9.	F9	0.989	0.951	0.965	0.975	0.981

Table 17: Table for regression coefficient and best fit kinetic model.

Sr. No.	Batch code	Regression coefficient (R)	Best fit model
1.	F1	0.958	Zero Order
2.	F2	0.985	Zero Order
3.	F3	0.980	Zero Order
4.	F4	0.980	Zero Order
5.	F5	0.976	Zero Order
6.	F6	0.981	Zero Order
7.	F7	0.986	Zero Order
8.	F8	0.981	Zero Order
9.	F9	0.989	Zero Order

Diclofenac sodium at pH 1.2. Sustained release of drug was displayed by all formulations in phosphate buffer. The sustained release of drug of batch F4, F5, F6 was found to be 92.52±0.973 %, 90.63±2.2191%, and 87.57±1.8801% respectively for a period of 10 hr, where as the formulation the sustained release of drug of batch F7, F8, F9 not more than 80% within 10hr because of comparatively high concentration of polymer.

Table 16 shows application of various kinetic models to the dissolution profile. From the data it can be conclude that zero order kinetics is best fit model for dissolution study.

Table 17 shows application of various kinetic models to the dissolution profile. From the data it can be conclude that zero order kinetics is best fit model for dissolution study.

Data treatment for optimization study

3 D Plot

The data clearly indicate that the values of drug release are strongly dependent on the selected

independent variables. To demonstrate graphically the effect of release modifying polymers on the dissolution profile, contour plots and 3D graphs were generated. The 3D graph as shown in Figure 9. The % drug release at 10 hrs is plotted on Y axis where as the concentration of independent variable (i.e TSP and MCC) were plotted on X and Z axis. As the concentration of TSP and MCC increased from 25 to 75 mg and 70 to140 mg respectively, the % drug release decreased signifying that the polymers have definite effect on drug release; especially along the axis region of TSP the effect was greater and prominent.

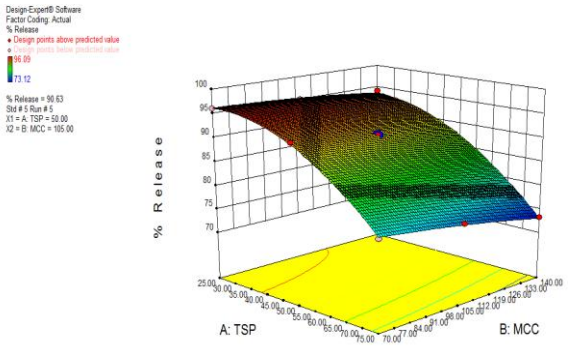

Figure 9: 3D graph plot showing amount of % drug release at tenth hour using different combination of TSP and MCC.

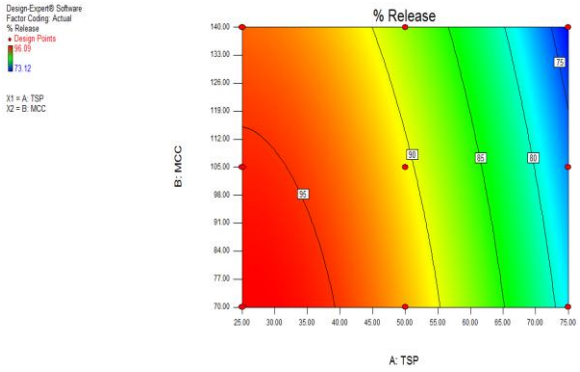

Figure 10: Contour plot showing amount of drug release at tenth hour (Y1) using different combination of X1, X2 The contour lines showing percentage of drug release at the end of tenth hour.

The contour plot

As shown in Figure 10 for % Drug release at 10 hrs justifies that optimum formulation complying with the acceptance criteria can be achieved by selecting the formulations near to the center of the triangle shaped contour plot which is the diagram obtained from the evaluation result of (F1 to F9) formulations. Almost similar results were observed with 3D graph and contour plot for release at 10hr. Here the major effect on the drug release was due to TSP.

Statistical analysis

Statistical optimization was carried out in design expert software (version 8.0.6.1.), which suggested that linear model was followed for release at 10 hrs with p-value of 0.0005. This indicated the model was highly significant. Therefore, linear model was selected for percent release at ten hours.In order to find out contribution of each components and their interaction, Analysis of Variance (ANOVA) was carried. Table 18 shows the results of the analysis of variance (ANOVA), which was used to generate mathematical models. The model F-value (35.59) implied the model was significant. Value of probability (p) less than 0.05, indicate model terms were significant. In this case, linear mixture components, A and B were significant model terms (where, A = TSP, B = MCC). The equation for percent drug release at the end ten hour:

Y1= +87.09 +8.00* A[1] +3.15* A[2] +1.86* B[1] +0.29* B[2] -0.86* A[1]B[1] +0.42 * A[2]B[1] -0.34* A[1]B[2] +0.10* A[2]B[2]

Table 18: ANOVA for selected statistical models.

Sr. No.	Response model	Release at 10 hrs
1.	Sum of Squares	574.32
2.	Degree of Freedom	2
3.	Mean Square	287.16
4.	Model F Value	35.59
5.	P Value	0.0005
6.	R Square	0.9223

Search for optimum formulation

Based on acceptance criteria and desirability factor Design Expert (Version 8.0.6.1) suggested

two optimum formulations OF1, OF2 has been shown in Table 19. The value of desirability closest to 1 is considered most favourable. The value of desirabilities for two optimized formulations OF1 and OF2 were 1. Optimized batches were formulated with the suggested composition. The pre and post compression parameter shown in Table 20 of optimum formulations showed good flow properties and excellent compression characteristics.

Table 19: Composition for Optimum batch OF1 and OF2.

Sr. No.	Ingredients	OF1(mg)	OF2 (mg)
1.	Diclofenac Na	100	100
2.	TSP	52.81	54.35
3.	MCC	82.25	79.83
4.	Lactose	107.94	108.82
5.	Talc	5	5
6.	Magnesium stearate	2	2

Table 20: Pre and post compression properties of optimized formulations (OF1, OF2).

Sr. No.	Parameter	OFI	OF2
1.	Bulk density	0. 531± 0.019	0.541± 0.021
2.	Tapped density	0.596 ± 0.025	0.601 ± 0.027
3.	Angle of repose	25.30 ± 0.48	22.35 ± 0.59
4.	Carr's index	10.09± 0.203	11.06 ± 0.253
5.	Hardness	5.84 ± 0.09	5.74 ± 0.084
6.	Friability	0.319± 0.031	0.367 ± 0.046
7.	Weight variation	348.5 ± 0.85	348.2 ± 0.19
8.	Drug content	99.85 ± 0.15	99.25 ± 0.11
9.	Thickness (mm)	3.37 ± 0.01	3.19± 0.08

Table 21: Cumulative percent drug release for marketed and optimized batches.

Sr. No.	Cumulative Percent Drug Release			
	Time (h)	**Marketed**	**Optimized Batch(OF1)**	**Optimized Batch(OF2)**
1.	1	0.34±0.19	2.47±2.95	1.04±0.52
2.	2	1.74±0.29	7.19±1.16	6.57±0.44
3.	3	19.45±2.42	21.38±1.84	18.96±0.24
4.	4	42.6±0.22	45.14±1.44	44.97±0.16
5.	5	47.71±0.27	48.58±2.62	48.64±0.09
6.	6	57.52±2.21	57.35±1.14	59.83±1.21
7.	7	70.67±1.30	68.38±1.51	69.04±0.70
8.	8	75.31±1.30	74.96±0.84	74.34±0.38
9.	9	82.58±1.27	83.58±2.32	81.8±0.13
10.	10	90.68±0.54	90.27±0.05	90.18±0.21

Dissolution studies were carried out for optimized as well as marketed formulation. (Voveran – SR). The predicted values for these optimum formulations OF1 and OF2 at 10 hr were 91.001% and 90.16% respectively. In vitro dissolution study was carried out. The cumulative % drug release at 10 hr was found to be 90.27% and 90.18%. So it can be concluded that optimised batches obeys design expert characteristics.

Dissolution study of marketed product

Brand Name: Voveran-SR
The dissolution study was carried out by USP II method. Following table illustrate the result.

Table 22: Comparative study of *in-vitro* release of marketed tablet and selected batch.

Sr.No.	Time in Hrs	Marketed Tablet % C.R.	Selected Batch(OF1) % C.R.
1.	1	0.34±0.19	2.47±2.95
2.	2	1.74±0.29	7.19±1.16
3.	3	19.45±2.42	21.38±1.84
4.	4	42.6±0.22	45.14±1.44
5.	5	47.71±0.27	48.58±2.62
6.	6	57.52±2.21	57.35±1.14
7.	7	70.67±1.30	68.38±1.51
8.	8	75.31±1.30	74.96±0.84
9.	9	82.58±1.27	83.58±2.32
10.	10	90.68±0.54	90.27±0.05

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

Comparison of *in-vitro* release between marketed formulation and optimized formulation

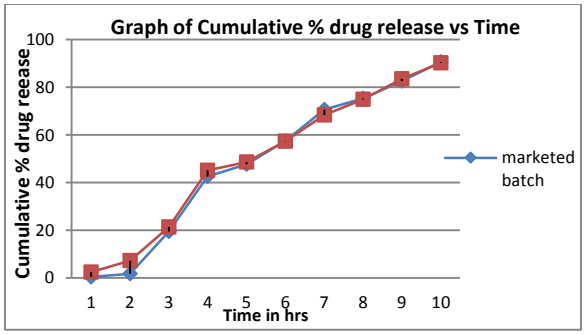

Figure 11: Dissolution profile marketed and optimized formulation.

Stability study

The optimized batch OF1 was kept for 4 week stability study. The results of stability study have been shown in Table 23. The results of dissolution profile of optimized formulation for different days have been shown in Table 24.

From the stability study and dissolution study data there is no significance change in characteristics of tablet formulation. So, it can be conclude that tablet passes the stability testing.

Tableting properties as well as pre and post compression studies of granules were carried out. It was found that, angle of repose and Compressibility Index (Carr's Index) of granules was found in the range of 25.98 ± 0.3 to 28.26 ± 1.81 and 7.11 ± 2.99% to 12.66 ± 1.245% respectively. It indicates excellent to acceptable flowability of granules. The drug content of each formulation was found to be uniform in the range of from 98.00 ± 0.98% to 99.9 ± 0.65% which passes the pharmacopoeial limit.

The *in-vitro* release study was carried out and revealed that cumulative % drug release in hydrophilic matrix tablet formulations were decreased with increase in concentration of polymer (TSP) This may be due to swollen polymer gel layer that was more thick as concentration of polymer increased, which was

Table 23: Stability study for final optimized batch OF1.

Sr.No.	Parameter	0 week	1 week	2 week	3 week	4 week
1.	Appearance	Off White	Off White	Off White	Off White	Off White
2.	Thickness	3.00±0.01	3.36±0.05	3.52±0.06	3.43±0.09	3.12±0.14
3.	Hardness	5.84±0.09	5.75±0.05	5.64±0.06	5.20±0.09	5.89±0.05
4.	Drug Content	99.85±0.15	99.3±0.45	99.4±0.53	99.4±0.82	99.80±0.95

Table 24: Dissolution study for optimized formulation.

Sr. No.	% Drug Release					
	Time	Initial	7 days	14 days	21 days	28 days
1	1	2.47±2.95	2.30±1.59	1.95±0.85	2.93±0.89	2.50±0.95
2	2	7.19±1.16	6.95±1.26	7.15±1.14	7.06±1.24	7.26±1.25
3	3	21.38±1.84	20.85±1.54	21.23±1.53	20.85±1.42	20.42±1.34
4	4	45.14±1.44	46.54±0.98	45..43±0.84	46.53±1.29	45.43±0.85
5	5	48.58±2.62	49.24±0.65	47.46±1.23	48.46±0.68	47.96±1.47
6	6	57.35±1.14	58.15±1.45	57.19±1.54	56.95±0.89	57.15±0.64
7	7	68.38±1.51	67.24±0.58	66.95±0.85	68.65±0.75	68.25±0.65
8	8	74.96±0.84	73.58±0.59	73.56±0.46	74.86±1.15	73.24±1.32
9	9	83.58±2.32	84.46±1.28	82.16±0.94	83.42±1.34	82.34±0.83
10	10	90.27±0.05	89.65±1.24	90.45±0.35	91.56±0.43	90.12±0.31

acting as barrier for release of drug .

Thus as polymer concentration increased the drug release was retarded in the order as F9 > F6>F1

The F1, F2, F3…F9 formulations could sustain the drug release up to 10 hours and more.

At the primary stage the swelling of the tablet takes place due to the absorption of water in to the matrix tablet. In later stages, due to penetration of more fluid, the viscous gel layer of hydrophilic polymer expanded considerably and acted as effective barrier for drug diffusion.

Formulation F1 to F9 could sustain the drug release up to 10 hour, But due to increasing concentration of the TSP in F7, F8, F9 formulation cumulative release only up to 78.24%, 76.47%and 73.12% respectively, Where as the F4, F5, F6 formulation sustain the drug release up to the 92.52%, 90.63% and 87.57% respectively which is comparatively match with marketed preparation among all F1to F 9 preparations.

Finally, the dissolution data for all trial formulations with different polymers was fitted into various kinetic models for depicting the mechanism of drug release of drug from the matrix tablets.

All Formulations F1, F2…..F9 of Diclofenac sodium has shown Zero order as best fit model. The natural polymers can used to modify the release rate of Diclofenac Na from matrix tablets. The extension of release profile depends on type of polymer, its physicochemical and physicomechanical properties as well as its concentration in the formula.

In swelling index study of the tablet as the polymer concentration increases, swelling index was found to increases. The swelling behavior indicated the rate at which this formulation absorbed water from dissolution media and swelled. It has been observed that the cumulative present drug release decreases with increasing concentration of the polymer.

All Formulations were found to be stable at room temperature for a period of one month. There was no appreciable change in the physical properties, drug content and dissolution studies during the testing period.

Conclusions

Tamarind seed polysaccharide can be employed in dosage form to sustain the drug release. Tablet formulated with various concentrations of Tamarind seed polysaccharide (TSP) gives release up to 10 h and more. OF1 and OF2 both formulations give comparable release with marketed formulation. From the present work it can be conclude that, the objectives which were set at the beginning of the study got fulfilled.

Funding: No funding sources
Conflict of interest: None declared

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