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FORMULATION AND *IN-VITRO* CHARACTERIZATION OF SUSTAINED RELEASE MATRIX TABLET OF DEXIBUPROFEN

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Keywords:

Dexibuprofen, Drug-excipients, FTIR, *In-vitro*, Methylcellulose, Sustained release matrix tablet

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ABSTRACT: Dexibuprofen is a Non-Steroidal Anti-Inflammatory Drug. It indicated short-term management of mild to moderately severe acute pain, dental pain, dysmenorrhoea, muscular pain and osteoarthritis. In the prevailing work, studies have been carried out on the preparation and in-vitro characterization of matrix tablets of dexibuprofen using different polymers like hydrophilic and hydrophobic. Different formulations had been prepared by wet granulation method using various release retarding polymers like methylcellulose, xanthan gum, and sodium carboxymethyl cellulose. Water-soluble surfactant sodium lauryl sulfate was employed to enhance the solubility of the dexibuprofen. Drug-excipients compatibility became performed by way of FTIR. Different parameters were evaluated for hardness, thickness, friability, drug content material, and *in-vitro* drug release. The excellent consequences were determined in terms of physicochemical parameters. The 10 numbers of formulations have been discovered to display the highest drug release of the drug. Mathematical analysis of the release kinetics has been accomplished to determine the mechanism of drug release. *In-vitro* release records have been fitted into diverse models to envision the kinetic of drug release.

INTRODUCTION: Non-steroidal anti-inflammatory drugs (NSAIDs) are contributors of a drug magnificence that reduces pain, decreases fever, prevent blood clots, and reduces inflammation [1, 2]. In standard, NSAIDs are characterized by way of a high degree of protein binding and small volumes of distribution [3]. In addition, dexibuprofen has verified comparable efficacy to diclofenac, naproxen, and celecoxib [4]. Dexibuprofen is an S (+)-isomer of ibuprofen, which is a chiral spinoff of 2-arylpropionic acid and demonstrates comparable therapeutic behaviour to different non-steroidal anti-inflammatory drugs (NSAIDs).

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It has been set up that management of ~200 mg of dexibuprofen produces equivalent analgesic effects to ibuprofen, but with a lower possibility of manufacturing adverse gastric effects [5]. Dexibuprofen **Fig. 1** belongs to BCS Class II of the drug compound because of its negative water solubility, which leads to variability in drug absorption and erratic bioavailability. It is mainly used to control mild-to-moderate ache and inflammatory situations, including headache, postoperative ache, dysmenorrhea, dental ache, and smooth tissue rheumatism [5, 6].

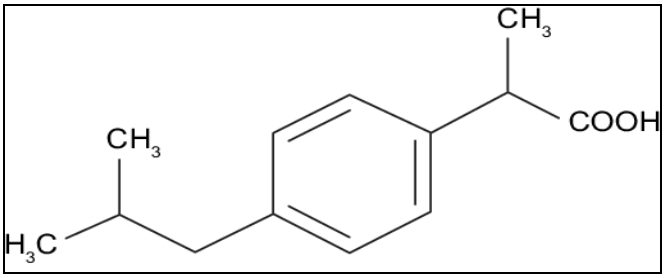

FIG. 1: CHEMICAL STRUCTURE OF DEXIBOPROFEN

A dose of 400 mg is effective in treating inflammatory situations, with the biological half-life of dexibuprofen being 1.8–3.5 h [7–9]. A dextrorotatory isomer of ibuprofen dexibuprofen is the pharmacologically effective enantiomer, released in Austria in 1994 [10]. Racemic ibuprofen and dexibuprofen differ in their physical, chemical, and pharmacological properties and their metabolic profile [11, 12].

In the last 5 years, 4836 patients have been uncovered to dexibuprofen in clinical trials and post-marketing surveillance (PMS) trials. Only in 3.7% of sufferers have adverse drug reactions been suggested and three extreme unfavorable drug reactions (0.06%) happened [11]. In the in vitro version, it has been demonstrated that dextrorotatory isomer famous approximately a hundred and sixty instances better activity in prostaglandins inhibition in assessment to enantiomer (R). Other research of thromboxane technology in clotting blood also showed better activity of enantiomer S than racemate [13]. Therefore, it'd be tremendously fine to apply dexibuprofen as an ache reliver. Especially, due to the reality that whilst dexibuprofen efficaciously inhibits the activity of COX-1 and COX-2, the enantiomer (R) demonstrates the inhibition handiest in the direction of COX-1 it's far really worth noting that it's miles accountable growing the aspect results in the gastrointestinal tract [14]. The negative water solubility of the drug results in a low dissolution rate, with subsequent partial and inconsistent absorption, limiting the drug exposure at its active site and constraining its clinical effectiveness [15].

Additionally, poor patient compliance has been observed for poorly water soluble drugs due to the need to deliver higher doses, with consequent large unit dose sizes making them tough to swallow. This will increase the cost of therapies and reduce their business elegance, even as the range in drug exposure typically related to products of this nature might have bad results and gain/chance profiles [16, 17]. Generally available techniques for addressing problems of low aqueous solubility in pharmaceutical development consist of particle size reduction, micronization [18], hot-melt extrusion technology [19], solid dispersions [18], nanoemulsions [19], microencapsulation [20], micelles [21], salt formation and complexation [22].

MATERIAL AND METHOD:

Material:

TABLE 1: LIST OF METERIALS USED

S. no.	Materials	Sources
1	Dexibuprofen	Indian finechemicals, Mumbai
2	Xanthangum	Indian finechemicals, Mumbai
3	Methylcellulose	Indian finechemicals, Mumbai
4	Sodium CMC	S. Dfinechemicals Limited, Mumbai
5	Micro-crystallinecellulose	Indian fine chemicals, Mumbai
6	Sodiumlaurylsulphate	MerckspecialitiesPvt.Ltd, Mumbai
7	Magnesiumstearate	Centraldrughouse Pvt. Ltd, New Delhi
8	Talc	S. Dfinechemicals, Mumbai
9	Sodiumhydroxide	FisherScientific, Mumbai
10	Potassiumdihydrogenphosphate	Qualigensfinechemicals, Mumbai

Method: In formulation development in this work, the wet granulation method was adopted with the aid of retarding agents to prepare sustained release matrix tablets of dexibuprofen.

The development of the formulation in the present was mainly based on the type and concentration of polymers. Dexibuprofen tablets were manufactured by wet granulation method using polymers like xanthan gum, methylcellulose and sodium carboxy methylcellulose (Sod.CMC). All the compositions in Table II (except magnesium stearate and talc) were thoroughly mixed by mortar and pestle for 15 min.

The powder mixture was granulated with the required amount of alcoholic solution of ethanol. The wet mass was passed through sieve # 16, and the granules were dried at 50^{o}C for 2 h in a hot air oven. The dried granules were passed through sieve # 20 and lubricated with magnesium stearate by further blended for 3 min, and finally, talc was

added to the blend. The mixed blend of drug and excipients were compressed to produce convex-faced tablets of 250 mg using 8 mm round punches on a multi-punch tablet compression machine. A batch of 50 tablets was prepared for each of the designed formulations.

TABLE 2: FORMULATION OF SUSTAINED RELEASE MATRIX TABLETS OF DEXIBUPROFEN

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Dexibuprofen	50	50	50	50	50	50	50	50	50	50
Xanthangum	50	100	-	-	-	-	-	-	-	-
Methylcellulose	-	-	50	100	-	-	50	100	-	-
Sodium CMC	-	-	-	-	50	100	-	-	50	100
Sodiumlauryl sulphate	-	-	-	-	-	-	2.5	2.5	2.5	2.5
MCC	142.5	92.5	142.5	92.5	142.5	92.5	140	90	140	90
Magnesiumstearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	5	5	5	5	5	5	5	5	5	5
Total(mg)	250	250	250	250	250	250	250	250	250	250

Data of *In-vitro* Drug Release Studies:

TABLE 3: *IN-VITRO* DRUG RELEASE PROFILE OF DEXIBUPROFEN FOR FORMULATIONS F1 TO F10

Time (hrs)	Cumulative % of Drug release									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0.5	1.32	1.45	2.19	1.67	1.45	1.39	21.84	14.70	16.68	10.36
1	4.85	4.85	6.98	6.41	6.03	6.15	28.41	21.61	25.21	20.90
2	6.80	7.16	8.72	8.33	7.56	7.92	37.16	28.49	36.21	25.18
3	8.61	8.54	13.24	11.89	8.47	13.78	41.05	33.79	38.97	32.18
4	12.42	13.15	16.17	15.63	9.46	15.82	47.34	40.81	41.44	41.46
5	14.33	16.78	22.19	18.90	10.85	20.67	53.59	49.40	48.83	48.08
6	16.58	20.33	30.33	24.39	11.78	23.34	56.57	57.73	54.07	56.90
7	19.96	23.12	32.81	26.48	17.75	26.79	64.17	64.88	61.06	63.77
8	22.95	25.06	38.54	34.30	24.47	30.33	73.65	72.60	65.90	73.98
9	25.16	29.21	40.90	40.04	31.61	33.45	78.35	78.44	74.73	78.78
10	30.27	31.97	42.83	41.57	38.01	38.30	85.26	84.28	76.03	85.33
11	35.00	34.16	47.23	44.08	41.13	39.57	94.16	90.11	89.66	91.96
12	37.20	36.50	48.47	45.63	43.01	41.67	95.44	94.43	95.59	97.85

RESULTS:

Precompression Evaluation Parameters:

Physical appearance: Physical appearance of the drug was examined by organoleptic properties, and the results are obtained as follows:

Colour: White or almost white.

Odour: Slight characteristic odour.

State: Crystalline powder.

The sample of dexibuprofen possesses similar colour, odour, and texture as given by officials; this supports the purity and authenticity of the drug.

Determination of Melting point: The melting point of the obtained sample was found to be 51^{o}C.

Determination of Solubility:

TABLE 4: SOLUBILITY OF DEXIBUPROFEN

S. no.	Solvents	Solubility
1	Distilled water	Insoluble
2	Ethanol	Soluble
3	Methanol	Soluble
4	Phosphate buffer (6.8)	Slightly soluble

Infrared Spectral Assignment: The drug's pellet of approximately 01 mm diameter was prepared to grind 3-5 mg of the sample with 100-150 mg of Potassium Bromide using the hydrostatic press.

The sample pellet was mounted in an IR compartment and scanned at wavelength 4000-500 cm^{-1}. The results were shown in **Fig. 2.**

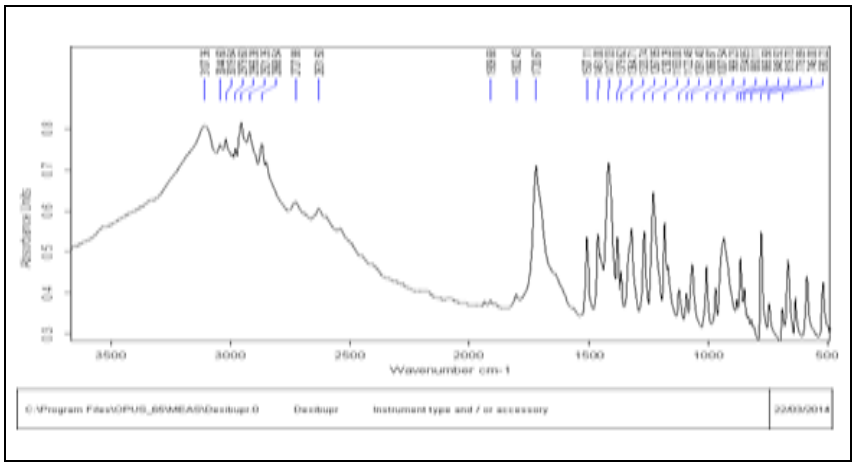

FIG. 2: FTIR SPECTRA OF DRUG (DEXIBUPROFEN)

TABLE 5: INTERPRETATION OF PURE DEXIBUPROFEN

Functional group	Wave number(cm^{-1})	Presence of peak
O-H group	3107.36	Present
C-H group	2955.38	Present
C=O group	1720.67	Present
C-C group	1417.03	Present
C-O stretching	1230.28	Present
O-H bending	778.89	Present

Ultraviolet Absorption Maxima: Ultraviolet absorption in the range of 200 to 400 nm of a 100 µg/ml solution of Dexibuprofen in phosphate buffer (pH 6.8) was scanned. The absorption maximum (λ_{max}) of Dexibuprofen was found be 222 nm which is shown in **Fig. 3.**

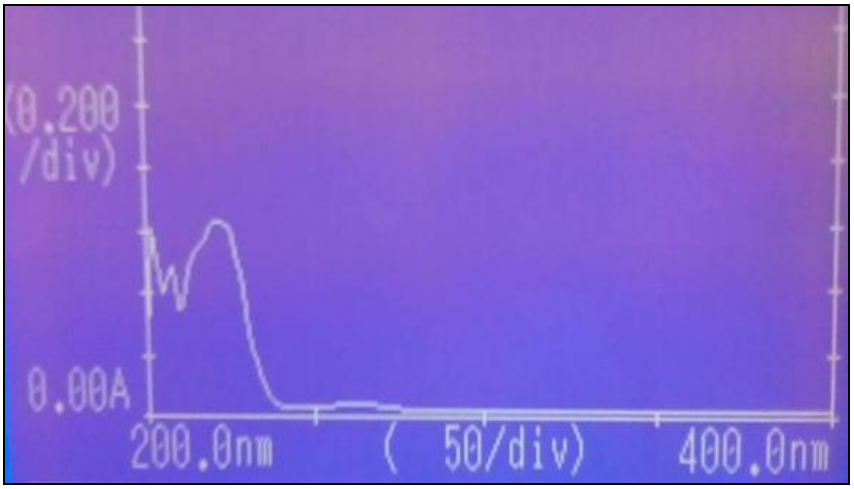

FIG. 3: SCAN OF DEXIBUPROFEN

Result of Calibration Curvedata: The calibration curve of dexibuprofen turned into prepared in phosphate buffer (pH 6.8).

The plot of various concentrations of dexibuprofen versus absorbance was observed to be linear in the concentration range of 10-50 µg/ml at 222 nm. The absorbance at different concentrations was proven in **Table 4**. The statistics of the preferred curve were linearly regressed. The slope and correlation coefficient values have been observed to be 0.0118 and 0.999, respectively. The calibration curve turned into proven in **Fig. 4.**

TABLE 6: CALIBRATION CURVE DATA OF DEXIBUPROFEN

S. no.	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	10	0.124
3	20	0.245
4	30	0.356
5	40	0.465
6	50	0.601

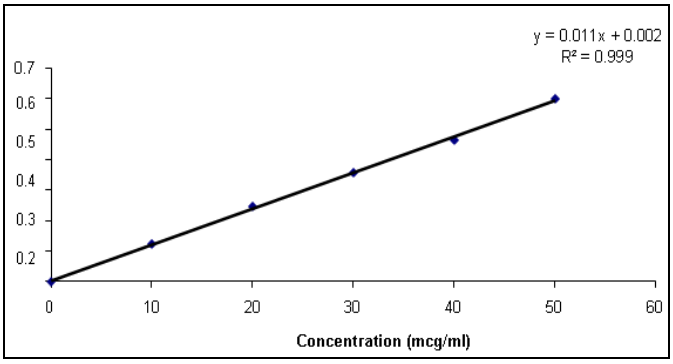

FIG. 4: CALIBRATION OF DEXIBUPROFEN

CONCLUSION: The objective of the present study was to formulate and examine a sustained release drug delivery system for a non-steroidal anti-inflammatory drug. This study prepared sustained release drugs with release retarding polymers and evaluated for numerous *in-vitro* parameters. Sustained release matrix tablets had been prepared by way of wet granulation technique the usage of distinctive polymers like xanthan gum, methylcellulose, sodium CMC. Solubility of dexibuprofen became more advantageous by way of using water-soluble surfactant SLS to acquire the preferred release. The tablets had been evaluated for his or her organoleptic (colour, odour), physical (size, shape and texture) and quality control parameters (thickness, weight variation, hardness, friability and *in-vitro* release). Dexibuprofen was analyzed for spectral (FTIR, UV) properties. The received effects of dexibuprofen had been concordant with reference specs of FTIR.

The outcomes showed no interaction between the drug dexibuprofen and the polymers employed in the formulation. Among all the formulations, F10 confirmed a higher drug release over 12 h of time, and it released over 97.95% of the drug out of 10 formulations with a sustained effect. Data of *in-vitro* drug release have been healthy into exclusive equations and kinetic model to explain the release kinetics of dexibuprofen from the sustained release tablet. On experimental records, it turned into concluded that sustained release matrix tablets of dexibuprofen could be a powerful alternative technique for managing aches. Sodium CMC and SLS proved to be the maximum promising dosage shape for sustained release of dexibuprofen drugs. It was also found that there was no interaction among the drug and polymer in all the formulations. Stability studies were conducted according to ICH guidelines for excellent formula F10 for a length of 3 months. The acquired consequences have been in the specification at both refrigerator and Long-term conditions and out of specification at the improved situation. Among all formulations, the optimized formula F10 fulfilled all the targets.

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