https://doi.org/ 10.33472/AFJBS.6.Si2.2024.646-653

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Formulation, Characterization and Optimization of Fast Dissolving Tablet of Celecoxib

Mrs. Vaishali A. Adsare[1], Siddharth S. Kale[2], Snehal S. Kale[3], Darshan S. Kale[4], Siddhesh D. Vaidya[5], Rutuja R. Sonawane[6], Kiran C. Mahajan[7], Ganesh Y. Dama[8]

[1-7]Department of Pharmaceutics, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal- Junnar, Dist- Pune, Maharashtra 410504, India.

[8]Department of Pharmcognosy, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal- Junnar, Dist- Pune, Maharashtra 410504, India.

Corresponding Author: Mrs.Vaishali A. Adsare

Associate Professor, Department of Pharmaceutics, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal- Junnar, Dist- Pune, Maharashtra 410504, India.

Email – vaibhavikk@yahoo.co.in

Article History

Volume 6,Issue Si2, 2024

Received:11 Mar 2024

Accepted : 12 Apr 2024

doi: 10.33472/AFJBS.6.Si2.2024.646-653

ABSTRACT

This study aimed to enhance the solubility and dissolution rate of celecoxib, a COX-2 inhibitor known for its anti-inflammatory and analgesic properties, by formulating fast dissolving tablets (FDTs) using solid dispersion with polyvinyl pyrrolidone K30 (PVP-K30). Various ratios of celecoxib to PVP-K30 were investigated, with the 1:4 ratio yielding the highest solubility compared to the pure drug. The dissolution rate of the FDTs were assessed in 2% SLS solution, with the in-vitro release ranked based on the percentage of drug released after 50 minutes.

Overall, the study successfully demonstrated the formulation and evaluation of FDTs containing celecoxib utilizing solid dispersion techniques. The results indicated that FDTs incorporating celecoxib solid dispersions in a 1:4 ratio exhibited superior solubility compared to the pure drug. This formulation strategy aimed to achieve a supersaturated drug release, facilitating rapid absorption upon oral administration.

Keywords: Celecoxib, Fast Dissolving Tablets, Solid Dispersion, PVP-K30, SLS, Dissolution Rate

INTRODUCTION

Celecoxib is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits potent anti-inflammatory and analgesic action by specifically inhibiting the COX-2 enzyme, which is responsible for the synthesis of prostaglandins that cause pain, inflammation.

Celecoxib belongs to the second class of the biopharmaceutical classification system (BCS) due to its low solubility and high permeability. Celecoxib has very low solubility as a classified class 2 compound according to the biopharmaceutical classification system. Celecoxib is a selective COX-2 inhibitor used to

treat osteoarthritis, rheumatoid arthritis, acute painful primary dysmenorrhea, and other conditions[1]. However, its poor water solubility can lead to dissolution rate-limited absorption and lower disintegration. To address this issue, fast-dissolving tablets of celecoxib have been developed using the solvent evaporation method, specifically solid dispersion techniques[2].

Solid dispersion techniques are widely used to improve the dissolution rate of poorly water-soluble drugs by enhancing their solubility. These techniques involve dispersing the drug in a carrier, such as PVP-K30, and then evaporating the solvent to form a solid dispersion.

Polyvinyl pyrrolidone (PVP-K30) is a widely utilized carrier in solid dispersions due to its exceptional water solubility and a broad range of molecular weights, spanning from 10,000 to 700,000 Da. This polymer is favoured for enhancing drug solubility and dissolution rates in various formulations[3].

MATERIAL AND METHODS

Materials

Celecoxib was provided by Niksan Pharmaceutical Pvt. Ltd, Ankleshwer, Gujarat, India. All chemicals used in the formulation preparation were of analytical grade and used without further purification.

Methods

Colour / Odour

The drug sample was placed on butter paper and visually inspected for color and odor under light, aiding in its identification.

Melting Point

The melting point, determined by the Fusion or Capillary Tube Method, involves sealing a tube filled with a drug sample and a thermometer. Heating the sample until it liquefies, the temperature is noted as the melting point.

Determination of Absorption Maxima of Celecoxib

Celecoxib was quantitatively analysed using a UV spectrophotometer with a 2% SLS solution. A standard calibration curve was established by preparing a stock solution with a concentration of 1000 µg/ml in 2% SLS. Test solutions were then prepared by diluting the sample to concentrations of 2, 4, 6, 8, and 10 µg/ml, and their absorbance was measured at the λ max of 254nm.

Solubility Analysis

Test the solubility of a drug by placing a small quantity in a test tube and assessing its dissolution in various solvents such as distilled water, SLS, ethanol, and methanol. This experiment determines the drug's affinity to dissolve in different solvents, aiding in formulation and dosage considerations[4-6].

Preparation of Celecoxib solid dispersions by the Solvent evaporation method

The preparation of solid dispersions involved dissolving celecoxib and PVP-K30 in precise ratios of 1:1, 1:2, 1:3, and 1:4 in methanol-filled petri dishes. After 2 hours of room temperature evaporation, the solid masses were scraped, crushed, pulverized, and sieved through an 80-mesh sieve. Stored in sealed glass containers, these solid dispersions capitalize on the advantageous properties of PVP-K30, including its superb water solubility and variable molecular weight.

FTIR Analysis

The FTIR spectra of pure celecoxib, physical mixture, and solid dispersion at a 1:4 ratio were analysed using a SHIMADZU, FTIR spectrophotometer. The absence of interaction between celecoxib and the carriers in the solid dispersion preparation was confirmed as the principal IR absorbance peaks of celecoxib solid dispersions matched those of the pure drug[7].

Formulation of Celecoxib Tablets

Celecoxib fast-dissolve tablets were formulated using a solid dispersion method, incorporating croscarmellose sodium and crospovidone as superdisintegrants. F1 to F6 formulations, containing two polymers, were prepared alongside an antiadherent, lubricant, and lactose monohydrate. The tablet weight was adjusted to 250 mg. See Table 1 for formulation details[8].

Table 1. formulation of Celecoxib Tablet

Ingredient (mg)	F1	F2	F3	F4	F5	F6
S.D of Celecoxib	100	100	100	100	100	100
Croscarmellose	1.25	6.875	12.5	-	-	-
Crosprovidone	-	-	-	5	8.75	12.5
Magnesium stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Lactose	125	119.32	113.75	121.25	117.5	113.75
Sodium saccharine	1.25	1.25	1.25	1.25	1.25	1.25
PVP	12.5	12.5	12.5	12.5	12.5	12.5
Total weight	250	250	250	250	250	250

Pre-formulation parameters

Preformulation involves studying the physical and chemical properties of drug substances and excipients to create a stable, safe, effective dosage form. Powder flow properties are assessed by Angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio.

Bulk density:

Bulk density is an essential property of powder, calculated as the ratio of the mass of a powder sample to its volume, which is critical for designing a dosage form.

Bulk Density = Weight of the powder / Volume of the powder

Tapped density:

Tapped density is measured by filling a measuring cylinder with dried powders, tapping it 100 times, then recording the volume and weight.

Tapped Density = Weight of the powder / Tapped Volume of the powder[9]

Angle of repose:

The angle of repose is an indicator of powder flowability, determined by measuring the angle between the sloping side of a conical pile and the horizontal plane. The funnel method is commonly used, where a powder sample is poured through a funnel to form a cone.

$\Theta = \tan^{-1}$ (h/r)

Carr's index:

The Carr's Index, also known as the Compressibility Index, is a measure of the compressibility of a powder, calculated based on the ratio of the tapped density to the bulk density.

Carr's index=Tapped density – Bulk density x 100 Bulk density

Hausner's ratio:

The Hausner Ratio is calculated as the tapped density divided by the bulk density.

Hausner's ratio= Tapped density / Bulk density[10]

Evaluation of post-compression parameters of prepared tablets

Diameter and Thickness:

Tablet diameter and thickness measured with Vernier calliper. Thickness influenced by die diameter. Average value calculated from 10 selected tablets.

Hardness test:

The hardness of 10 tablets was measured using the Monsanto hardness tester. Hardness measured in kg/cm². Triplicate readings obtained, and average value calculated for accurate assessment.

Friability:

The friability of tablets was tested in a labline friabilator with 3 tablets, 4-minute duration, and 25 rpm speed.

% Friability = (W1-W2)100/W1[11]

Weight variation test:

As per the Indian Pharmacopoeia, weight variation testing involves individually weighing 10 tablets on a digital balance to determine the average tablet weight accurately.

In-vitro disintegration time:

The in-vitro disintegration test is performed with six tablets in distilled water containing 2% SLS w/v at 37°C as the disintegration medium. The time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus is measured in seconds.

In-vitro drug release study:

In vitro dissolution study of Celecoxib tablets was performed using the paddle method (USP Apparatus 2) to evaluate the drug release rate. The dissolution medium consisted of 900 mL of distilled water containing 2% SLS (w/v) maintained at 37 ± 1°C and rotated at 50 rpm. At different intervals of time, 5 mL samples were drawn and diluted suitably, then filtered and assayed spectrophotometrically at 254 nm[12].

RESULTS AND DISCUSSION

Determination of Absorption Maxima of Celecoxib

A calibration curve of celecoxib was plotted using distilled water containing 2% SLS (w/v) as the solvent, following the experimental method described. The standard graph of celecoxib showed good linearity with an R2 of 0.9996, indicating that it obeys Beer-Lambert's law. The calibration curve absorbance and graph shown in Table 2 and Figure 1.

Table 2: Standard calibration curve of celecoxib

Sr. No.	Concentration (µg/ml)	Absorbance at (254) nm
1	0	0
2	2	0.0701
3	4	0.1479
4	6	0.2183
5	8	0.2892
6	10	0.3559

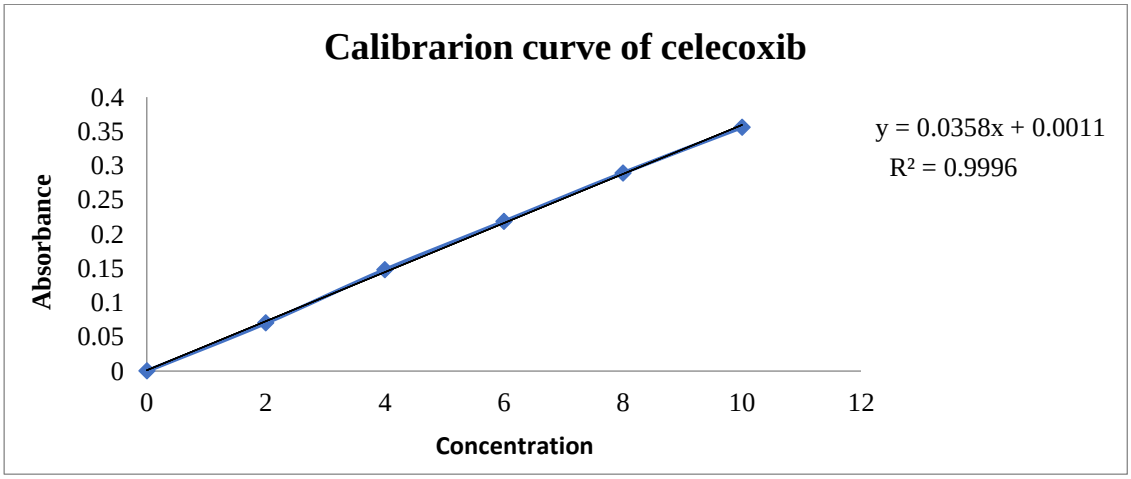

Figure 1: Calibration curve of Celecoxib

FTIR studies

FTIR spectroscopy examined drug-polymer interaction. Spectra of pure drug, solid dispersion, and physical mixture (Figures 2, 3, and 4) indicate no chemical reaction between them. FTIR spectra of celecoxib pure drug showed the following characteristic peak at 3232 cm-1 N-H stretching vibration Frequency, 1157 cm-1 S=O Sulphonamide Symmetric stretching vibration Frequency, 1641cm-1C=N Bending vibration Frequency, 1157 cm-1 CF3 Stretching vibration Frequency, 771 cm-1 C-H Aromatic Bending vibration Frequency, which is shown in figure 2.

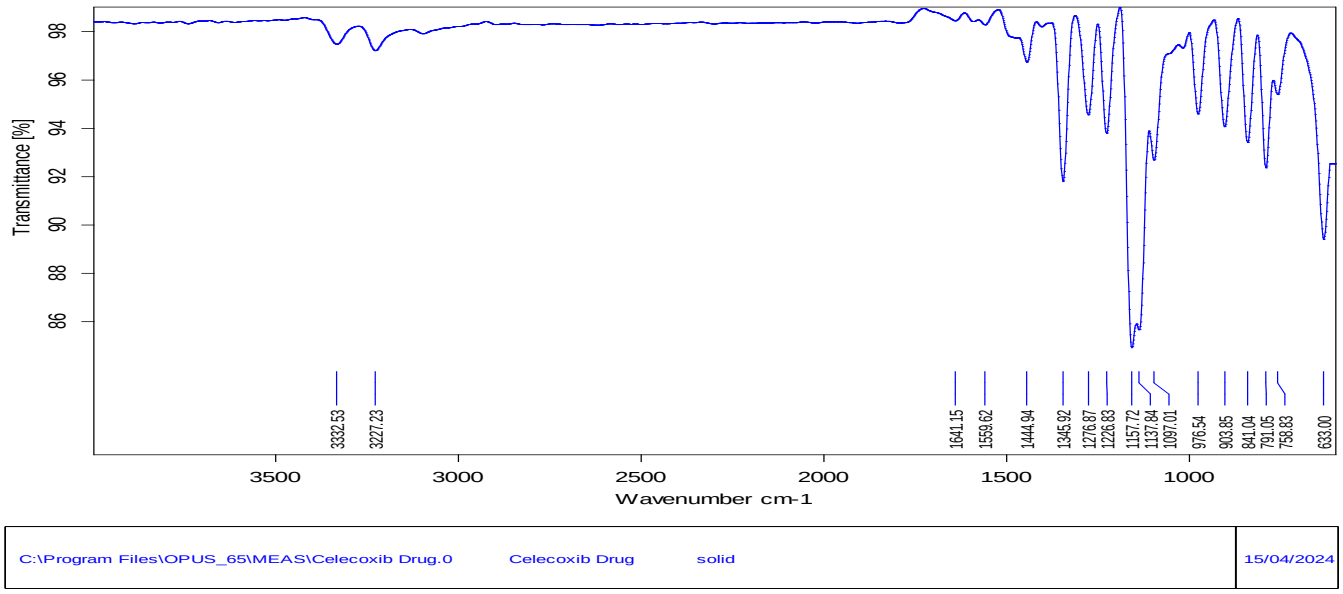

Figure 2: FTIR spectra of celecoxib pure drug

FTIR spectra of celecoxib solid dispersion showed the following characteristic peak at 3284 cm-1 N-H stretching vibration Frequency, 1154 cm-1 S=O Sulphonamide Symmetric stretching vibration Frequency, 1648 cm-1 C=N Bending vibration Frequency, 1154cm-1 CF3 Stretching vibration Frequency, 653cm-1 C-H Aromatic Bending vibration Frequency, which is shown in figure 3.

Figure 3: FTIR spectra of celecoxib solid dispersion

FTIR spectra of celecoxib physical mixture (F1 batch) showed the following characteristic peak at 3238 cm-1 N-H stretching vibration Frequency, 1142 cm-1 S=O Sulphonamide Symmetric stretching vibration Frequency, 1644 cm-1C=N Bending vibration Frequency, 1030 cm-1 CF3 Stretching vibration Frequency, 725 cm-1 C-H Aromatic Bending vibration Frequency, which is shown in figure 4.

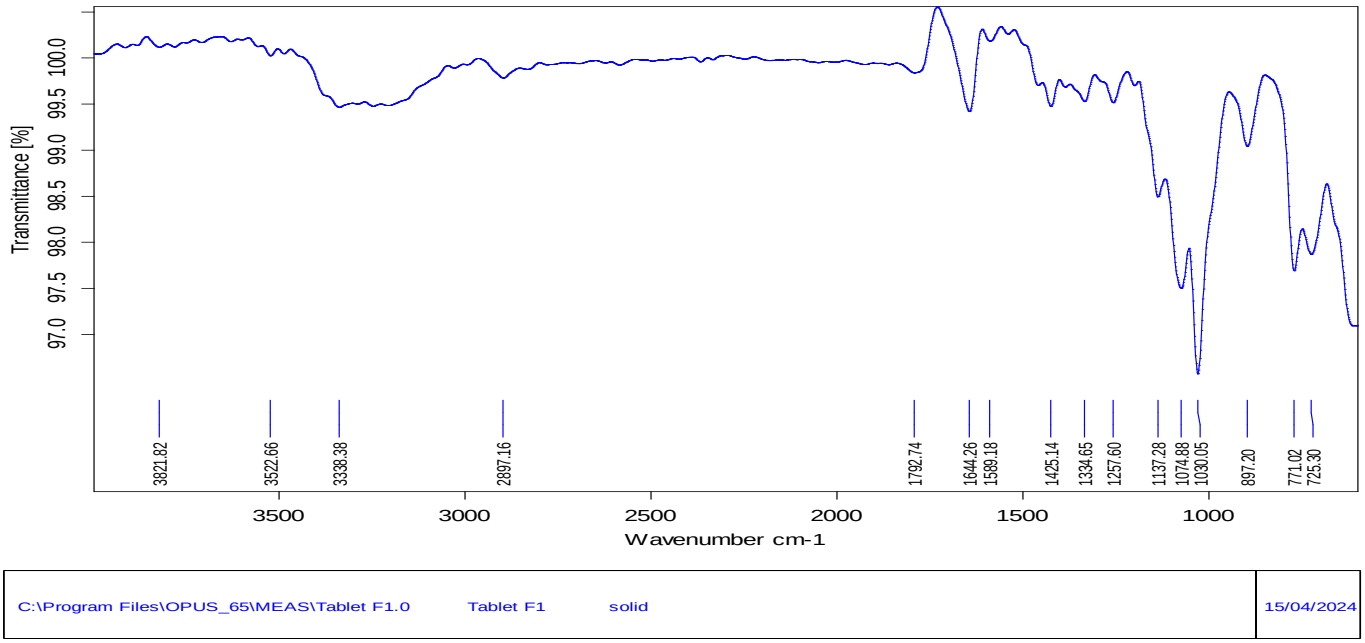

Figure 4: FTIR spectra of physical mixture (F1 batch)

Preformulation parameters:

The tablet's pre-compression parameters indicated bulk density ranging from 0.31 to 0.41 gm/cm3 and tapped density from 0.35 to 0.50 gm/cm3. Carr's index and Hausner's ratio showed no significant variations. The angle of repose, which indicates the flow properties of the powder, was obtained between 34.11 to 34.99 degrees, indicating good flow properties. Micromeritic studies, including bulk density, tapped density, Hausner's ratio, Carr's index, and angle of repose, met acceptable criteria across all formulations, as detailed in Table 3.

Table 3: pre-compression characteristics of Celecoxib SD with excipient

Formulation	Bulk density (gm/cm3)	Bulk density (gm/cm3)	Carr's Index (%)	Hausner's Ratio	Angle of repose
F1	0.357	0.4166	14.30	1.16	31.79
F2	0.4166	0.4345	8.33	1.09	34.60
F3	0.4166	0.500	16.68	1.20	30.11
F4	0.3125	0.3841	18.74	1.23	34.60
F5	0.3333	0.4166	19.99	1.24	32.61
F6	0.3125	0.3571	12.48	1.14	34.99

Evaluation of post-compression parameters of prepared tablets

The weight variation of the tablets was found to be within acceptable limits, with no significant difference from the average weight. The USP limits for tablet weight variation are less than 5% deviation from the average weight. The diameter of the tablets was in the range of 9-10 mm, and the thickness was between 3.6-3.78 mm. The hardness of the tablets ranged from 3.7-4.1 kg/cm2, and all formulations passed the USP requirements for friability and uniformity of weight. The in vitro disintegration time was found to be in the range of 26.5-38.4 seconds. All evaluation parameters shown in Table 4

Table 4: Evaluation parameters of Tablets

Formulation	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	disintegration time (sec.)
F1	248.26 ± 1.15	3.78	4.3	0.35	26.5
F2	248.74 ± 1.63	3.73	3.9	0.28	31.8
F3	246.88 ±2.97	3.7	3.7	0.26	29.4
F4	248.3 ±1.64	3.6	4.2	0.22	36.2

F5	249.75 ± 3.08	3.7	3.8	026	34.3
F6	248 ± 3.84	3.7	4.1	0.32	38.4

***In vitro* drug release study**

The *In vitro* drug release study of Celecoxib tablets was conducted using the paddle method (USP Apparatus 2) to evaluate the drug release rate. The dissolution medium consisted of 900 mL of distilled water containing 2% SLS (w/v) maintained at 37 ± 1°C and rotated at 50 rpm. The percentage drug release of all formulations from F1 to F6 were within the range of 96.97 – 99.54 % for 50 min. The results indicate that F1 had better drug release than the other formulations. The drug release study shown in Figure 5.

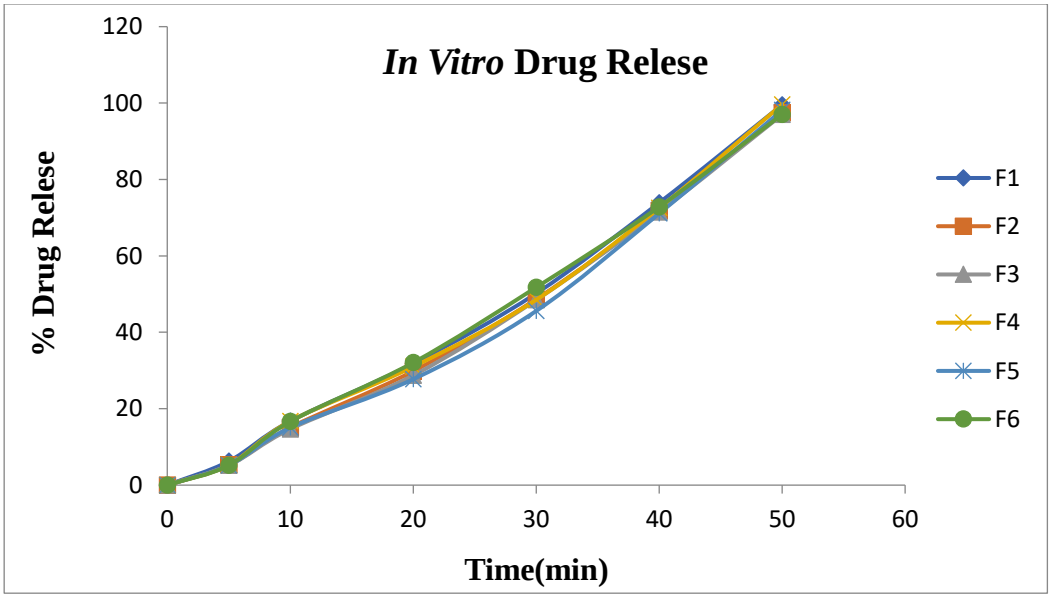

Figure 5*: In vitro* drug release of different batches

CONCLUSION

This study aimed to enhance celecoxib solubility and dissolution rate, a BCS II drug with poor water solubility, by creating solid dispersions with PVPK-30 via the solvent evaporation method. The resulting dispersion (F1 batch) achieved a remarkable 99.54% *in-vitro* drug release, demonstrating PVPK-30's efficacy as a carrier. Notably, a 1:4 ratio of celecoxib to PVP K-30 significantly improved both solubility and dissolution rate. The study also proposed the feasibility of preparing fast-dissolving celecoxib tablets using direct compression techniques with various superdisintegrants.

The optimized batch F1 (best batch) showed superior dissolution rates with croscarmellose polymer compared to crospovidone. In the dissolution study of the solid dispersion, the 1:4 ratio exhibited the highest dissolution rate and solubility. Sodium lauryl sulphate (SLS) emerged as a suitable dissolution medium for the solid dispersion of fast-dissolving tablets. The *In vitro* disintegration time was found to be less than 1min. Overall, this research underscores the potential of PVPK-30 as a carrier for enhancing celecoxib's solubility and dissolution rate, alongside promising avenues for the formulation of fast-dissolving tablets.

REFERENCES

[1] Muralidhar, G. Devala Rao, V. Rajesh Babu, T. Karunakar Reddy and Syeda Rana Nikhat. Fast dissolving celecoxib tablets containing solid dispersion of celecoxib. International Journal of Pharmacy and Pharmaceutical Sciences.2010, Vol. 1 (9): 34-40

[2] Alireza Homayouni, Fatemeh Sadeghi 1, Ali Nokhodchi, Jaleh Varshosaz , Hadi Afrasiabi Garekani . Formulation, Characterization, and in Vivo Evaluation of Celecoxib-PVP Solid Dispersion Nanoparticles Using Supercritical Antisolvent Process. Molecules 2014, 19(12), 20325-20339

[3] Hemant Agrawal, To prepare and evaluate orodispersible tablet of anti-inflammatory drug, World Journal of Biology Pharmacy and Health Sciences, 2022, 12(01), 165–173

[4] Laxmikant B.Dhande, Madhuri T. Deshmukh, Abhijit N. Khopade, Rajkumar V. Shete, Shanmukhappa C. Shetty, Formulation and Evaluation of Solid Dispersion of Celecoxib, Bull. Env. Pharmacol. Life Sci., Vol 10 [5] April 2021 : 81-91

[5] Daljit Masih, Rajesh Gupta, Formulation Development and In-vitro Evaluation of Mouth Dissolving Tablets of Celecoxib Employing Distinctive Proportion of Disintegrating Agents, UK Journal of Pharmaceutical and Biosciences Vol. 2(2), 16-21, 2014

[6] Singh B, Khurana LK, Handa M, Singh S. Development of fast dissolving tablets of Celecoxib using different techniques. International Journal of Pharmacy and Pharmaceutical Sciences. 2011;3(2):100-106.

[7] Patel D, Patel K, Patel M. Formulation and evaluation of fast dissolving tablets of Celecoxib. International Journal of Pharmaceutical Sciences and Research. 2013;4(10):3988-3993.

[8] Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. Journal of Controlled Release. 2009;139(2):94-107.

[9] Chaudhary SA, Singhai AK. Formulation and evaluation of fast dissolving tablets of Celecoxib. International Journal of Pharmacy and Pharmaceutical Sciences. 2013;5(1):348-354.

[10] Shah JS, Shah KR, Shah YP, Prajapati LP. Formulation and evaluation of fast dissolving tablets of Celecoxib using superdisintegrants. Asian Journal of Pharmacy and Life Science. 2012;2(1):186-197.

[11] Liew KB, Tan YTF, Peh KK. Formulation and evaluation of fast dissolving tablets of Celecoxib using different disintegrants. Tropical Journal of Pharmaceutical Research. 2013;12(2):227-234.

[12] Satpute N, Pimple S, Shinde A, Maheshwari D. Formulation and evaluation of fast dissolving tablets of Celecoxib using sublimation method. International Journal of Pharmacy and Pharmaceutical Sciences. 2016;8(9):174-179.