WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 14, Issue 21, 775-783. Research Article ISSN 2277–7105

DEVELOPMENT AND CHARACTERIZATION OF NOVEL MICROSPONGE GEL LOADED WITH KETOPROFEN FOR TRANSDERMAL DELIVERY

Vinay H. S.[1]*, Krishna K. R.[2], Parthiban S.[3]

Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya-571422.

Article Received on 01 Oct. 2025,
Article Revised on 22 Oct. 2025,
Article Published on 01 Nov. 2025,

https://www.doi.org/10.5281/zenodo.17472180

***Corresponding Author**

Vinay H. S.

Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya-571422.

How to cite this Article: Vinay H. S.*, Krishna K. R., Parthiban S. (2025). Development and Characterization Of Novel Microsponge Gel Loaded With Ketoprofen For Transdermal Delivery. World Journal of Pharmaceutical Research, 14(21), 775–783.

ABSTRACT

Aim: The study aimed to formulate and evaluate Ketoprofen-loaded microsponge and microsponge gel systems for sustained topical delivery. Preformulation studies including melting point, solubility, and λmax confirmed drug purity, while FTIR indicated compatibility of Ketoprofen with ethyl cellulose, validating its suitability for controlled release. **Methodology:** Microsponges were prepared using ethyl cellulose and PVA in varying ratios and evaluated for particle size, drug content, entrapment efficiency, and in vitro release. All formulations showed >85% drug content and entrapment efficiency, with F6 showing the highest values (92.39% and 91.37%). In vitro studies confirmed sustained release up to 8 hours, with F6 showing the most controlled release (87.1%). Kinetic analysis revealed Zero-order release and Super Case II transport. **Result:** Optimized microsponges were incorporated into gels showing smooth texture, stability, and pH 6.1–6.4. Viscosity (10,840–11,320 cps) and spreadability (6.50–7.02 cm) were within acceptable limits. In vitro drug release from gels showed prolonged release, with F6MG1 achieving 90.6% cumulative release following Zero-order kinetics. **Conclusion:** Ketoprofen-loaded microsponge gels were stable and effective, providing sustained drug release and showing potential as a controlled-release topical formulation for enhanced therapeutic efficacy.

KEYWORDS: Ketoprofen, Microsponge, Ethyl cellulose, PVA, Sustained release, Topical gel, Zero-order kinetics, Super Case II transport.

INTRODUCTION[1-4]

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It acts as a protective mechanism that alerts the body to harmful stimuli; however, when it becomes chronic, pain loses this protective role and significantly impairs quality of life. Chronic pain results from alterations in neural signaling pathways and remains a major therapeutic challenge. Advances in molecular pain research have identified specific therapeutic targets, such as selective cyclooxygenase-2 (COX-2) inhibitors, which provide effective analgesia with fewer adverse effects than traditional nonsteroidal anti- inflammatory drugs (NSAIDs).

Pain perception begins with the activation of nociceptors—specialized sensory neurons that respond to noxious thermal, mechanical, or chemical stimuli. During inflammation, chemical mediators such as prostaglandins, bradykinin, and histamine lower the activation threshold of these neurons, leading to heightened pain sensitivity. NSAIDs reduce prostaglandin synthesis through COX enzyme inhibition, thereby decreasing nociceptor sensitization and alleviating pain. In addition, they indirectly modulate ion channels such as TRPV1 and acid-sensing ion channels (ASICs), which play essential roles in transmitting pain signals.

Inflammation is a complex physiological response to tissue injury, infection, or irritation, characterized by redness, heat, swelling, and pain. It involves the release of mediators such as prostaglandins, cytokines, and histamine, which activate and sensitize peripheral nociceptors. Among these mediators, prostaglandins are key contributors to pain and edema. NSAIDs act by inhibiting COX-1 and COX-2 enzymes, thereby preventing prostaglandin formation, reducing inflammatory cytokine release, and minimizing leukocyte migration to the affected area. Consequently, NSAIDs are widely used for the management of inflammatory and musculoskeletal disorders, arthritis, and soft tissue injuries.

Transdermal drug delivery systems (TDDS) have gained attention as an alternative route for both local and systemic drug administration. These systems provide controlled and sustained drug release through the skin, bypassing hepatic first-pass metabolism and improving bioavailability and patient compliance. Drug permeation mainly occurs via transcellular, intercellular, and appendageal routes, with the stratum corneum serving as the primary barrier. TDDS offer several advantages, including reduced systemic side effects and prolonged therapeutic action, but are limited to potent drugs with favourable physicochemical properties and may occasionally cause skin irritation.

Microsponges are highly porous, polymeric microspheres that can entrap active ingredients and release them in a controlled manner. Their structure allows sustained drug release at the target site while minimizing irritation and maintaining therapeutic concentrations for extended periods. Microsponges are stable, non-irritant, and compatible with a wide range of formulations. They are prepared mainly by liquid–liquid suspension polymerization or quasi-emulsion solvent diffusion techniques and have found applications in topical, oral, and cosmetic formulations.

Gels are semisolid systems that offer localized drug delivery with good patient acceptability. Their biocompatible matrix ensures effective drug retention and sustained release at the site of application. Microsponge-loaded gels combine the advantages of both systems— controlled drug release from microsponges and the ease of application and spreadability of gels. Such formulations enhance drug stability, reduce dosing frequency, and improve therapeutic outcomes in the treatment of inflammatory and musculoskeletal conditions.

MATERIALS AND METHODS[5-11]

Pre formulation studies

Preformulation studies of Ketoprofen were performed to confirm its identity, purity, and compatibility with excipients. The melting point determined by the capillary method complied with standard values. The drug showed maximum absorbance at 260 nm in phosphate buffer pH 7.4, confirming its λmax. FTIR analysis revealed no significant drug–excipient interactions, indicating compatibility for formulation development.

PREPARATION OF KETOPROFEN MICROSPONGE BY QUASI EMULSION SOLVENT DIFFUSION METHOD

Drug loaded micro-sponges will be prepared by quasi emulsion solvent diffusion method. The internal phase consisted of Ethyl cellulose in dichloromethane. The drug (250 mg) was gradually added to the ethyl cellulose solution with continuous stirring at 800 rpm. The internal phase is then added dropwise into the aqueous external phase containing polyvinyl alcohol. After 2 hrs. of stirring, the micro-sponges will be formed by evaporation of dichloromethane from the system. The micro-sponges will be filtered and then dried in hot air oven at 40 °C till constant weight and store in airtight container.

Table 1: Composition of Ketoprofen microsponges.

Formulation code	F1	F2	F3	F4	F5	F6
Ketoprofen (mg)	250	250	250	250	250	250
Ethyle cellulose (mg)	250	500	750	250	500	750
Dichloromethane (ml)	10	10	10	10	10	10
Water (ml)	100	100	100	100	100	100
PVA (mg)	125	125	125	250	250	250
Stirring time (hrs.)	2	2	2	2	2	2

EVALAUATION OF MICROSPONGES

Determination of production yield

$$\% \text{ of production yield} = \frac{\text{Practical mass of microsponge}}{\text{theoritical mass (drug + polymer)}} \times 100$$

Particle size distribution

Particle size analysis of prepared microsponges was carried out by using optical microscopy method. The calibrated microscope was used to count approximately 100 microsponges.

Entrapment efficiency

$$\%\text{Entrapment efficiency} = \frac{\text{Experimental drug content}}{\text{Theoretical drug content}} \times 100$$

Drug content

Ketoprofen content in microsponges was assayed by an UV spectrophotometric method. Microsponges containing equivalent to 10 mg of drug were dissolved in a 100 ml phosphate buffer of pH 7.4 After suitable dilution absorbance was measured by UV spectrophotometer against blank at λmax 260 nm and drug content was calculated.

In vitro release study

In vitro release pattern of microsponges was carried out in dissolution apparatus USP Type 1 using phosphate buffer pH 7.4 as dissolution medium with a modified basket consisted of 5µm of stainless-steel mesh. Ketoprofen containing microsponges equivalent to 100 mg was taken in the basket. The speed of the rotation is 50 rpm and temperature of 37± 0.5°C. At fixed intervals, aliquots 5 ml sample were withdrawn periodically and were replaced by fresh buffer. The samples were assayed by UV spectrophotometer at 260 nm using phosphate buffer pH 7.4 as blank and % CDR was calculated and plotted against time.

RESULTS AND DISCUSSION

The characterization of pure Ketoprofen confirmed its identity, purity, and physicochemical properties using UV-visible spectroscopy, FT-IR, and DSC. The melting point was observed at 104°C, within the reported range of 100–110°C, confirming the drug's purity. Solubility studies showed that Ketoprofen is freely soluble in water, ethanol, acetone, chloroform, propylene glycol, PEG 400, and phosphate buffers at pH 4.4, 6.8, and 7.4, indicating suitability for formulation in various solvent systems. The λmax was recorded at 260 nm in pH 7.4 phosphate buffer, and the calibration curve exhibited linearity (R^2 = 0.9991) over a concentration range of 3–15 µg/ml, demonstrating the reliability of the UV spectrophotometric method for quantitative analysis. FT-IR analysis confirmed that the characteristic functional groups of Ketoprofen were retained in the physical mixture with excipients, indicating compatibility and absence of significant drug–excipient interactions.

Microsponge formulations (F1–F6) were evaluated for particle size, drug content, entrapment efficiency, and in vitro drug release. Particle sizes ranged from 135.39 nm (F6) to 147.34 nm (F3), suggesting uniform microsponge formation at nanoscale. SEM images revealed spherical and porous microsponges, beneficial for controlled drug release. Drug content ranged from 85.86% to 92.39%, and entrapment efficiency varied from 86.73% to 93.36%, with F6 showing the highest values. In vitro release studies demonstrated sustained drug release over 8 hours, with cumulative release from 87.13% to 92.59%, confirming effective prolonged delivery. Kinetic modelling showed that formulations followed the Peppas model with "n" values >1, indicating Super Case-II transport, while high correlation coefficients for zero-order kinetics ($R^2 \approx 0.998–0.999$) confirmed uniform drug release.

Overall, the results indicate that Ketoprofen retains its chemical integrity in the presence of excipients, ensuring stability in the formulation. The nanosized porous microsponges allow for efficient drug entrapment and sustained release, minimizing dose frequency. The optimized formulation F6 exhibited the highest drug content, entrapment efficiency, and controlled release, making it a promising candidate for oral delivery. The study demonstrates that the designed microsponge system effectively improves Ketoprofen's solubility, stability, and release profile, highlighting its potential for enhanced therapeutic efficacy and patient compliance.

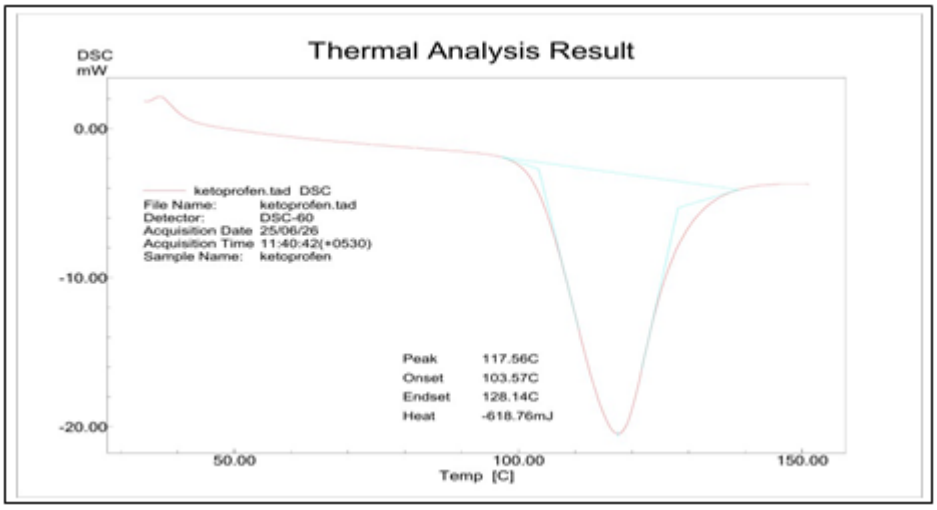


Figure 1: DSC Thermograph of Ketoprofen.

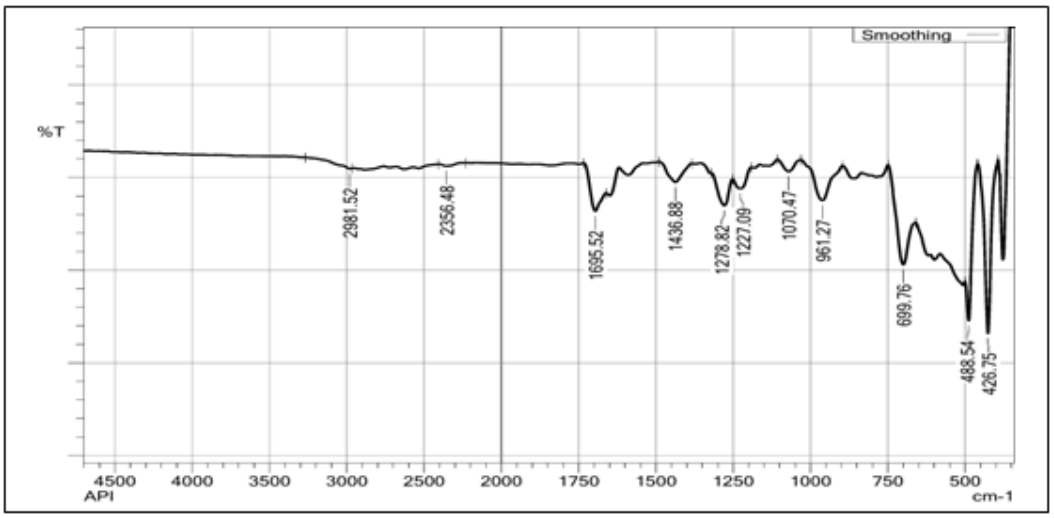


Figure 2: FT –IR spectra of pure Drug.

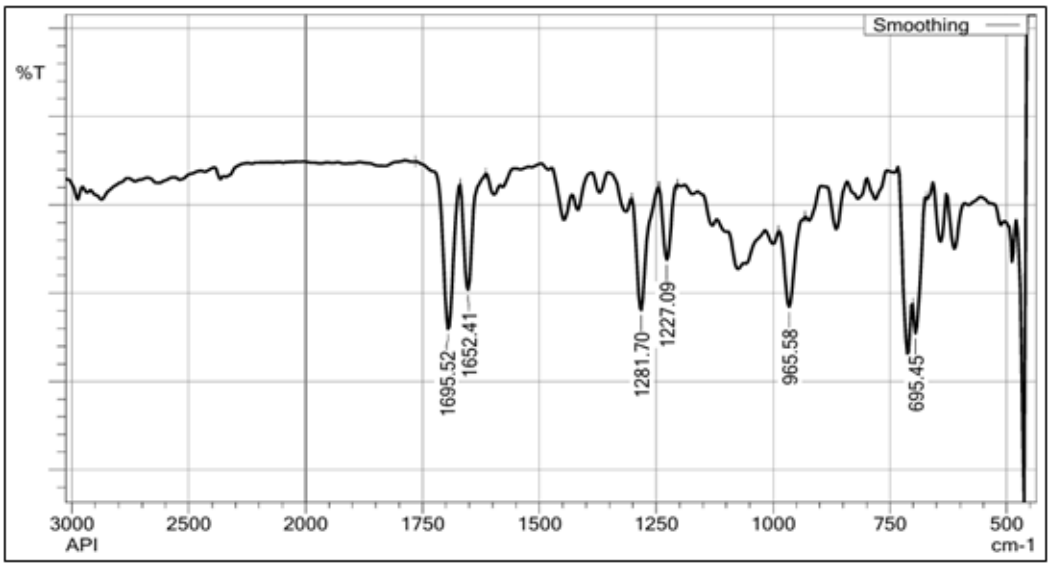
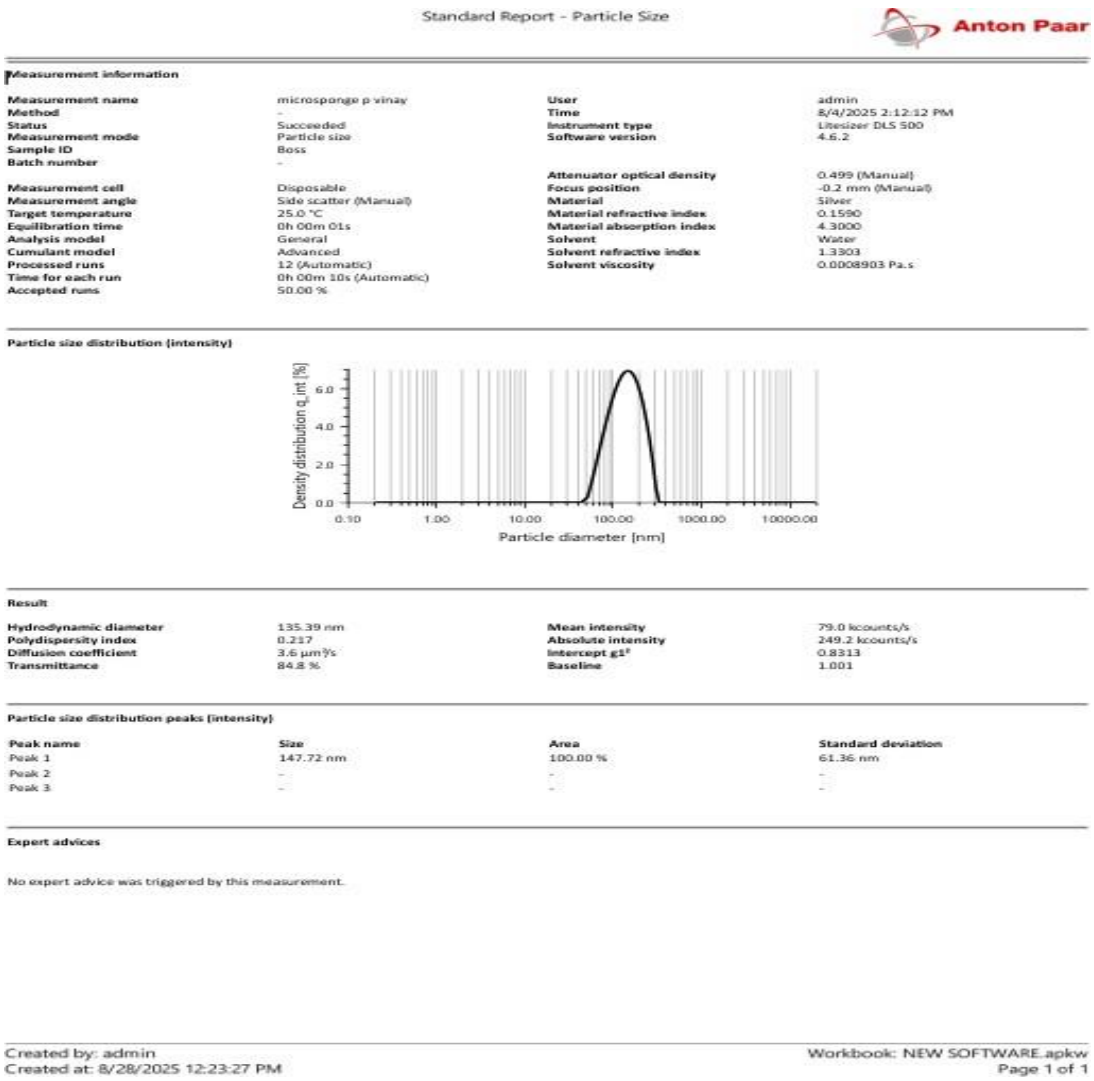


Figure 3: FT-IR spectra of physical mixture I: Drug + Ethyl cellulose.



Standard Report - Particle Size

Anton Paar

Measurement information

Measurement name	microsponge p vinay	User	admin
Method	-	Time	8/4/2025 2:12:12 PM
Status	Succeeded	Instrument type	Litesizer DLS 500
Measurement mode	Particle size	Software version	4.6.2
Sample ID	Boss		
Batch number	-		
		Attenuator optical density	0.499 (Manual)
Measurement cell	Disposable	Focus position	-0.2 mm (Manual)
Measurement angle	Side scatter (Manual)	Material	Silver
Target temperature	25.0 °C	Material refractive index	0.1590
Equilibration time	0h 00m 01s	Material absorption index	4.3000
Analysis model	General	Solvent	Water
Cumulant model	Advanced	Solvent refractive index	1.3303
Processed runs	12 (Automatic)	Solvent viscosity	0.0008903 Pa.s
Time for each run	0h 00m 10s (Automatic)		
Accepted runs	50.00 %		

Particle size distribution (intensity)

Result

Hydrodynamic diameter	135.39 nm	Mean intensity	79.0 kcounts/s
Polydispersity index	0.217	Absolute intensity	249.2 kcounts/s
Diffusion coefficient	3.6 µm²/s	Intercept g1²	0.8313
Transmittance	84.8 %	Baseline	1.001

Particle size distribution peaks (intensity)

Peak name	Size	Area	Standard deviation
Peak 1	147.72 nm	100.00 %	61.36 nm
Peak 2	-	-	-
Peak 3	-	-	-

Expert advices

No expert advice was triggered by this measurement.

Created by: admin
Created at: 8/28/2025 12:23:27 PM

Workbook: NEW SOFTWARE.apkw
Page 1 of 1

Figure 4: Particle size analysis of optimized formulation F6.

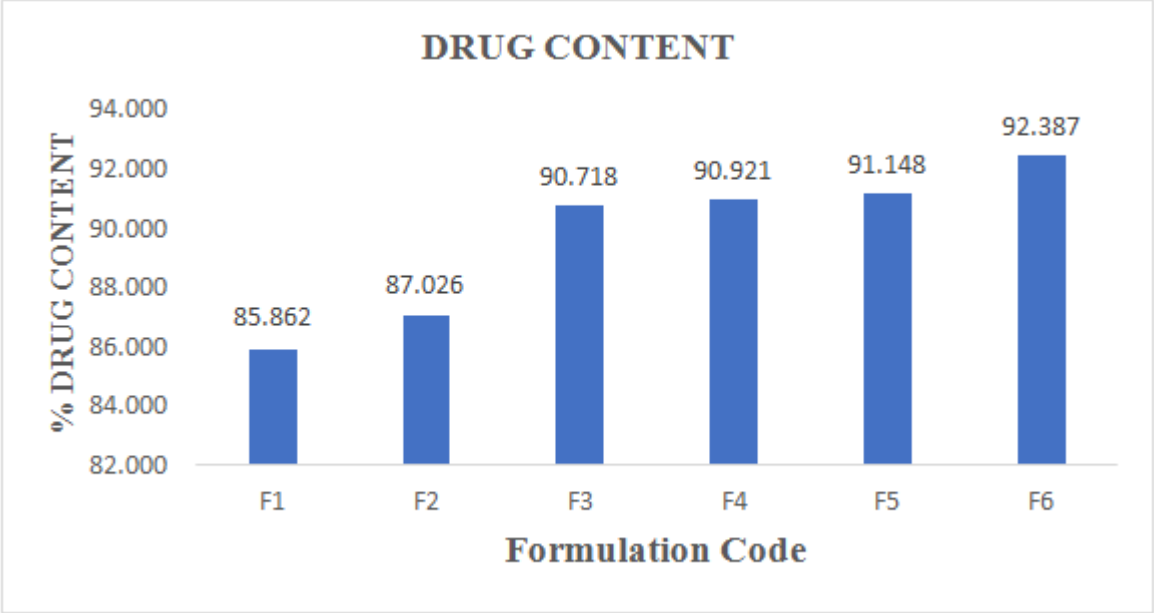


Figure 6: % Drug content of F1-F6 formulation.

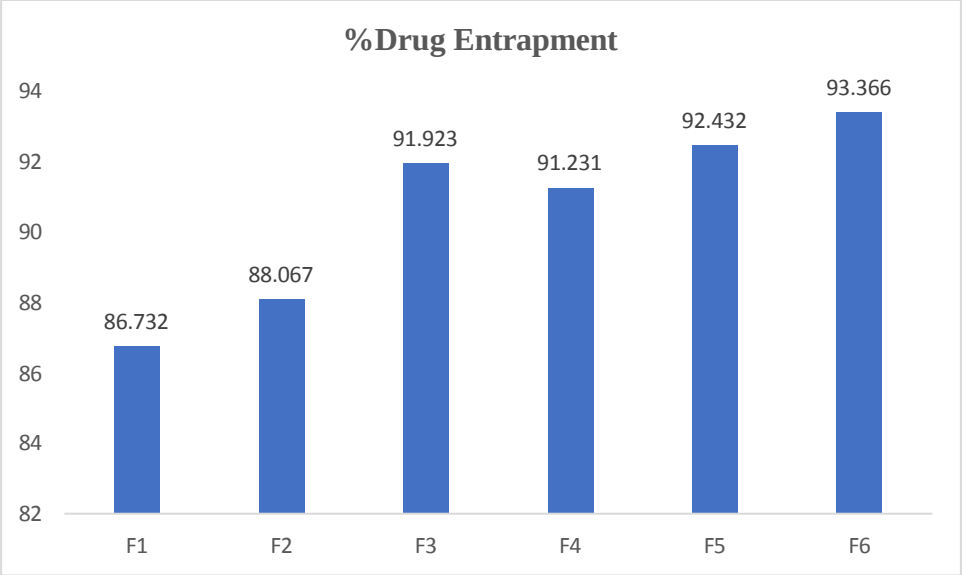


Figure 7: % Drug entrapment efficiency F1-F6.

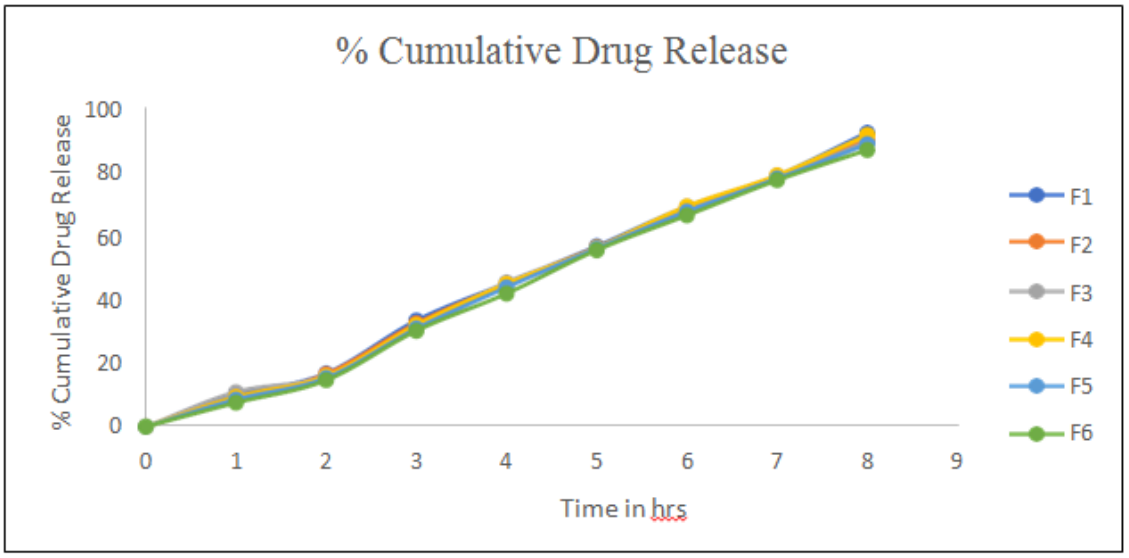


Figure 8: *In vitro* drug release profile of F1-F6 formulation.

CONCLUSION

The study confirmed the identity, purity, and stability of Ketoprofen using UV, FT-IR and DSC, with a melting point of 104°C and λmax at 260 nm. The drug was freely soluble in various solvents and compatible with excipients. Microsponge formulations (F1–F6) showed uniform nanosized particles, high drug content (85.86–92.39%) and entrapment efficiency (86.73–93.36%), with F6 as the optimized formulation. In vitro studies demonstrated sustained release over 8 hours following Peppas kinetics, indicating effective controlled delivery. Overall, the microsponge system enhanced Ketoprofen's solubility, stability, and release profile, making it a promising oral delivery system for improved therapeutic efficacy and patient compliance.

REFERENCE

1. Neural Plasticity and Disorders of the Nervous System. Cambridge University Press. Pain, 2006; 149–24.
2. Arunachalam A, Karthikeyan M, Kumar DV, Prathap M, Sethuraman S, Ashutoshkumar S, Manidipa S. Transdermal drug delivery system: a review. Journal of Current Pharma Research, 2010 Oct 1; 1(1): 70.
3. Thakur R, Kumar S, Gaba P. A review: Novel method for microsponge drug delivery system. J Pharm Biol Sci., 2020; 15(4): 35-44.
4. Patan A, Sangheshett. Microsponge in drug delivery: A review. Int J Parenter Dermatol., 2017; 1(1): 32-39.
5. Pavani U. The development and evalutionof nanosponges drug delivery system of ketoprofin by using solvent evaporation method. J cardiovasc Dev dis Research, 2021; 12(4): 970-77.
6. Uddin R, Sansare V. Design, Fabrication and Evaluation of Ketorolac Tromethamine Loaded Microsponge Based Colon Targeted Tablet. Int J Adv Pharm Biotechnol., 2020; 1(6): 2-4.
7. Rohith G, Satheesha Babu BK. Influence of chitosan thioglycolic acid conjugate in improving bioavailability of an antiparkinson drug; Rasagiline Mesylate from transdermal patch. Drug Dev Ind Pharm., 2021; 47(6): 963-76.
8. Vernekar A, Gude R, Ghadi N, Parab S, Shirodker A. Formulation and characterization of controlled release flurbiprofen Microsponges loaded in gels Ind J Pharm Edu Res., 2019; 53(1): 50- 58.
9. Balamurugan K, Kshirsagar N, Govardhan P. Microsponges: as a drug delivery system. J Pharm Innov., 2019; 8(1): 139-43.
10. Vitthal P and Anuradha S. A review on microsponges drug delivery system. Int J Res Anal Rev., 2020; 7(1): 961-74.
11. Dineshmohan S, Gupta VR. Transdermal delivery of fluconazole Microsponges: Preparation and *in vitro* characterization. J Drug Deliv Ther., 2016; 6(6): 7-15.