IJPSR (2022), Volume 13, Issue 3 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 13 June 2021; received in revised form, 12 August 2021; accepted, 15 August 2021; published 01 March 2022

STUDIES ON SOLID DISPERSION OF CURCUMIN USING HYDROPHILIC POLYMER WITH SYLOID XDP AND LOZENGE CHARACTERIZATION

Pradnya Palekar Shanbhag *, Supriya Lande and Saima Shaikh

Department of Pharmaceutics, Oriental College of Pharmacy, Sector No. 2, Plot No. 3, 4, 5, Sanpada West, Navi Mumbai - 400705, Maharashtra, India.

Keywords:

Curcumin, Syloid XDP, PVP K30, Internal ternary solid dispersion, Lozenges, Antibacterial, *Streptococcus aureus*

Correspondence to Author:
Dr. (Mrs.) Pradnya Palekar Shanbhag

Department of Pharmaceutics, Oriental College of Pharmacy, Sector No. 2, Plot No. 3, 4, 5, Sanpada West, Navi Mumbai - 400705, Maharashtra, India.

E-mail: drpradnyaps@gmail.com

ABSTRACT: Curcumin, an active phytochemical compound of the rhizome Curcuma longa, shows several pharmacological activities. Curcumin shows high permeability and low dissolution rate, and its incomplete absorption leads to very poor oral bioavailability. The present study aimed to enhance curcumin's solubility and dissolution rate by forming internal ternary solid dispersion using hydrophilic polymer PVP K30 and water-insoluble surface modifying carrier Syloid XDP in a weight ratio of 1:3:2, 1:3:3, 1:1:3, and 1:2:2 for curcumin: PVP K30: Syloid XDP. Saturation solubility of internal ternary solid dispersion showed many folds increase in solubility as compared to plain curcumin in water, pH 1.2, 4, 6.8, and 7.4. Lozenges prepared from internal ternary solid dispersion showed excellent solubility and dissolution comparable with the marketed product. The lozenges exhibited improved antibacterial activity and rapid drug dissolution for a prolonged period of time. Therefore, they can be a promising alternative to the marketed product as immunity booster, anti-inflammatory, and oral hygiene. The study suggests that internal ternary solid dispersion of curcumin prepared using PVPK30 and Syloid XDP can be used to improve solubility and dissolution desired for bio enhancement.

INTRODUCTION: Curcumin (1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-dione) is a hydrophobic polyphenol derived from the rhizome of turmeric Curcuma longa [1, 2]. Curcumin has good biological activities and pharmacological actions, such as anti-inflammatory, anti-angiogenic, anti-tumor, anti-oxidation [1, 3, 4].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(3).1338-43

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(3).1338-43

It shows no significant toxicity in humans at several grams orally daily and for months. It is also accounted that curcumin is safe and sounds up to 8 g/day [5, 8]. However, according to the Bio pharmaceutics Classification System (BCS), curcumin belongs to a Class II drug that is poorly water-soluble but highly permeable [1, 9, 10].

The oral bioavailability of a drug depends on its solubility and/or dissolution rate, and dissolution may be a rate-determining step for medicinal effect; therefore, efforts to increase drug dissolution with limited water solubility are often needed. Many methods are developed to improve these characteristics, including salt formation, micronization and solvent or surface-active agents

[5, 11]. Solid dispersion is one of the promising techniques for improving an effective surface area of poorly water-soluble drugs. Major principles of solid dispersion to improve drug solubility include: (a) solid dispersion of a drug with the inert carrier (highly water soluble) in contact with water gets dissolved, leaving behind suspension of drug in a microcrystalline form gets absorbed rapidly [12]. (b) enhanced surface area and conversion of the crystalline form of the drug into its amorphous form [13]. Water-soluble carriers and water-insoluble carriers have been used to improve the dissolution rate of drugs. Water-soluble carriers being moisture-sensitive create handling problems compared to water-insoluble carriers [11]. Solid dispersion may give rise to stickiness and/or tackiness due to water-soluble polymeric carriers. Surface modifying carriers such as porous silica materials decrease the crystallinity of drugs and therefore show higher drug dissolution rates [14].

In the present research work, Triple "C" solid dispersion system, called an internal ternary solid dispersion (ITSD) system, represents a promising approach that includes benefits of conventional solid dispersion and surface solid dispersion by virtue of adsorption property of porous fine silica materials. Syloid XDP has been chosen as an innovative drug carrier with a rationale, as smaller particle size (50 μm) provides greater internal surface area (300 m2/g), enabling to improve the dissolution rate of drug due to its highly adsorptive nature and high pore volume (1.7 ml/g) [15].

MATERIALS AND METHODS: The materials were received as gift samples. Curcumin (95% purity, Konark Herbals Ltd, India), Syloid® XDP (average particle size of ∼50 μm, Grace Davison Chemicals India Pvt. Ltd., India), Sucrex (Gangwal Chemicals Pvt. Ltd., **India**), F-Melt C (Gangwal Chemicals Pvt. Ltd., India), Plasdone® K-30 (BASF). Other ingredients were purchased from HiMedia, Mumbai, India.

Preparation of Curcumin-Internal Ternary Solid Dispersions: Curcumin-Internal Ternary Solid Dispersions (Cur-ITSDs) were prepared to improve aqueous solubility of curcumin using polymer PVP K30. Homogeneous clear solutions of curcumin and PVP K30 were prepared in ethanol in the ratios 1:1, 1:2, and 1:3. The clear solutions were heated gently at 45 ºC until half of the solvent evaporated. The carrier, Syloid XDP was added to the above clear concentrated solutions in the ratio of curcumin: PVP K30: Syloid XDP as 1:3:2, 1:3:3, 1:1:3, 1:2:2. After suspending the carrier, it was mixed thoroughly, and excess solvent was removed by gently heating at 45 ºC. The complex was sieved through 60 mesh SS sieve. The Cur-ITSD system was stored in a dehumidifying chamber at room temperature.

Saturation Solubility of Cur-ITSD: The saturation solubility of Cur-ITSD was determined by using an orbital shaker at 200 rpm for 24 h at 37 ºC. Apparent solubility was determined in distilled water, pH 1.2, 4, 6.8 and 7.4. An excess amount of the samples (10 mg) was dispersed in 5 ml of distilled water, pH 1.2, pH 4, pH 6.8 and pH 7.4. After 24 h of shaking, samples were filtered through 0.2 μm membrane filter, and the filtrate was diluted with the respective medium. The absorbance was recorded using a UV-visible spectrophotometer at λ 428 nm.

Drug Content of Cur-ITSDS: 750 mg of sample was weighed accurately and dissolved in 25 ml ethanol. The solution was sonicated for 20 min and then centrifuged at 4000 rpm for 10 min. 0.1 ml of supernatant was diluted with a suitable quantity of ethanol.

The absorbance of the supernatant solution was recorded at λ 428 nm using a UV-visible spectrophotometer and the drug content was determined using the calibration curve of absorbance versus concentration.

Differential Scanning Calorimetry (DSC): DSC analysis was performed using a scanning calorimeter (Hitachi 7020). 10 mg of samples were weighed and sealed in aluminum pans. The samples were scanned at 10 ºC/min from 30 ºC to 300 ºC under the nitrogen purge gas flow rate of 25 ml/min and the thermal behavior was studied by recording the thermograms.

Fourier Transform Infrared Spectroscopy (FTIR): FTIR spectra of samples were performed on IRSpirit FTIR spectrophotometer. The scanning range was 500-4500 cm^{-1} and the resolution was 4 cm^{-1}.

Development of Lozenges of Cur-ITSD: Lozenges were prepared of Cur-ITSDs using standard excipients. All excipients, including Cur-ITSD, were sieved through 60 mesh SA sieve and mixed by the geometric dilution method for 10 min. Lozenges were prepared by direct compression technique using Rotary Compression Tablet Press with 12.7 mm flat punch and total weight 750 mg per lozenge with hardness 9 kg/sq.cm. Compressed lozenges were evaluated for standard evaluation parameters, drug content, in-vitro disintegration time, in vitro dissolution study, and antimicrobial activity. The composition of lozenges is shown in **Table 1.**

TABLE 1: FORMULATION COMPOSITION OF CUR-ITSD LOZENGES

S. no.	Ingredients	F1 (%)	F2 (%)	F3 (%)	F4 (%)
1.	Curcumin: PVP K30: Syloid XDP	79.99	93.33	66.66	66.65
2.	F-Melt C	14.95	1.61	28.28	28.29
3.	Sucrex	2	2	2	2
4.	Flavor	1.06	1.06	1.06	1.06
5.	Sodium stearyl fumarate	2	2	2	2

Optimized formulation was evaluated for drug content, in vitro disintegration time and in vitro drug release and compared with marketed product of curcumin.

Drug Content of Lozenges: Lozenges were taken randomly and crushed in a mortar. Powder weight equivalent to one lozenge was dissolved in ethanol, and volume made up to 25 ml. The solution was sonicated for 10 min. The above solution was diluted with a suitable quantity of ethanol. The absorbance of the solution recorded at λ 428 nm using a UV-visible spectrophotometer was used to determine the concentration.

***In-vitro* Disintegration Time:** *In-vitro* disintegration time was determined using disintegration apparatus. Lozenges were placed in the tubes of the device containing 900 ml distilled water, and the time taken for the lozenges to disintegrate completely at 37 ºC was noted.

***In-vitro* Dissolution Study:** *In-vitro* dissolution study was carried out using six station USP Apparatus Type II in 900 ml of 0.1 N HCl with 1% SLS at 75 rpm for 6 h at 37 ± 0.5 ºC. Lozenges were placed in each of the vessels of the dissolution apparatus containing the medium. 5 ml aliquots were withdrawn at specified time intervals of 1, 2, 3, 4, 5 and 6; and same amount was replaced by fresh medium. The withdrawn aliquots were suitably diluted and analyzed through UV-visible spectrophotometer at λ 428 nm. All studies were carried out in triplicates.

Antimicrobial Study: Antibacterial activity of optimized formulation was examined using a bacterial strain of *Staphylococcus aureus*. Petri plates containing nutrient agar were prepared. Bacterial culture was spread over the petri plates according to the spread plate technique. Filter paper discs were cut in 8 mm diameter. The aqueous solution of the optimized formulation was placed on the disc and allowed it for proper diffusion. The discs were placed in the above petri plates. The plates were kept in the incubator for 24 h at 37 ºC. The test was performed in triplicates. The zone of inhibition was measured after 24 h.

RESULTS AND DISCUSSION: Hydrophilic carriers such as PVP K30 used in preparing solid dispersion of curcumin helps to improve the wettability of hydrophobic surfaces of the drug particle. PVP K30 has an excellent surface stabilizing effect and prevents the molecular association from forming a protective coat around the drug particle, thus rendering hydrophilicity on the drug particle surface. Syloid XDP increases drug loading in solid dosage forms.

It helps to release the drug quickly and completely from the dosage form and thus improves the bioavailability of hydrophobic actives. Syloid XDP shows a higher dissolution rate because of the ability to decrease the crystallinity of the drug. Saturation solubility of Cur-ITSDs showed many folds increase in solubility as compared to plain curcumin in all the media, as shown in **Table 2.** Solubility profile was dependent on both PVP K30 and Syloid XDP concentrations. An increase in solubility of curcumin might be due to hydrophilic nature of PVP K30 along with Syloid XDP that enhances dissolution rate. The drug content of different batches was found to be uniform and within acceptable range from 98.5% to 98.937%.

TABLE 2: SATURATION SOLUBILITY & DRUG CONTENT OF CUR-ITSDS

Media	Saturation solubility (mcg/ml)				
	Plain Curcumin	Cur-ITSD (1:3:2)	Cur-ITSD (1:3:3)	Cur-ITSD (1:1:3)	Cur-ITSD (1:2:2)
Purified Water	0.264	30.24	25.6	20.7	33.36
pH 1.2 (0.1 N HCl)	0.132	12.58	9.42	5.22	14.56
pH 4.0	0.198	13.9	10.65	8.44	15.8
pH 6.8	0.595	18.2	16.4	14.25	20.39
pH 7.4	0.728	59.24	55.3	50.24	65.47

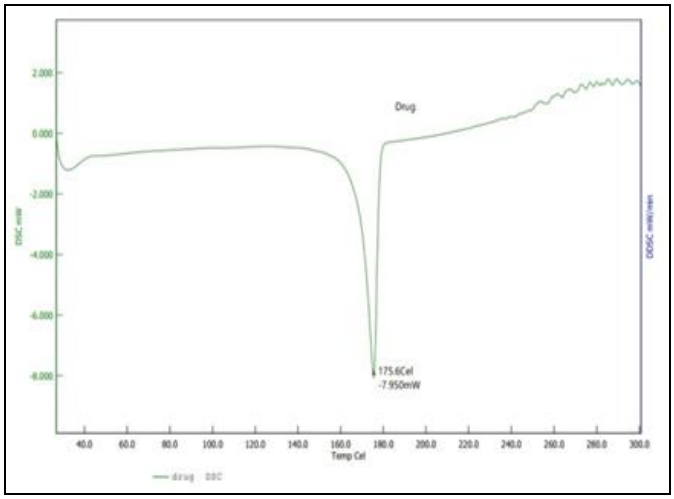

FIG. 1: DSC OF CURCUMIN

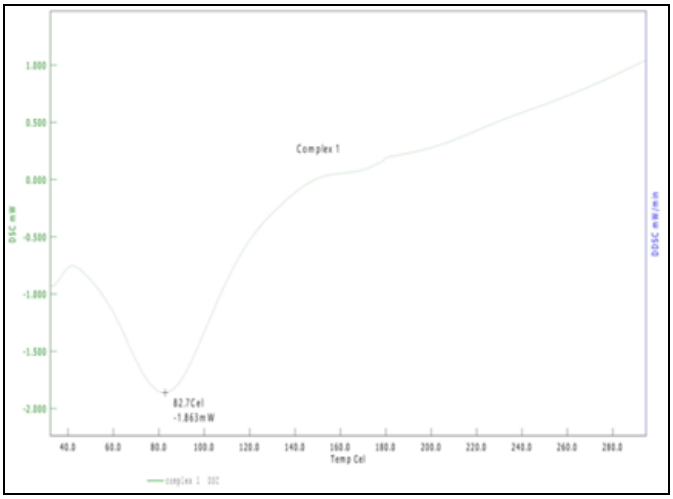

FIG. 2: DSC OF CUR-ITSD

FTIR spectroscopy helps to determine any interaction between PVP K30 and Syloid XDP with curcumin. FTIR spectrum of plain curcumin showed a stretching vibration at 3450 cm^{-1} indicating the presence of O-H group and at 1650 cm^{-1} indicating the presence of C=O group, as seen in **Fig. 3.** The FTIR spectrum of Cur-ITSD was similar to plain curcumin with no significant difference in the spectrum, as seen in **Fig. 4.**

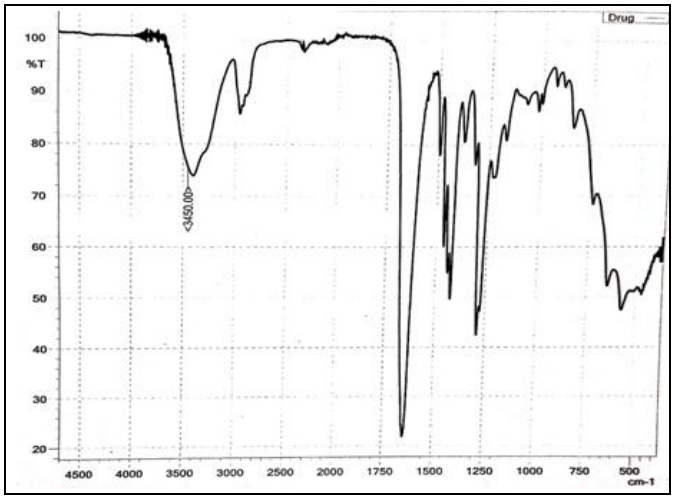

FIG. 3: FTIR SPECTRA OF PLAIN CURCUMIN

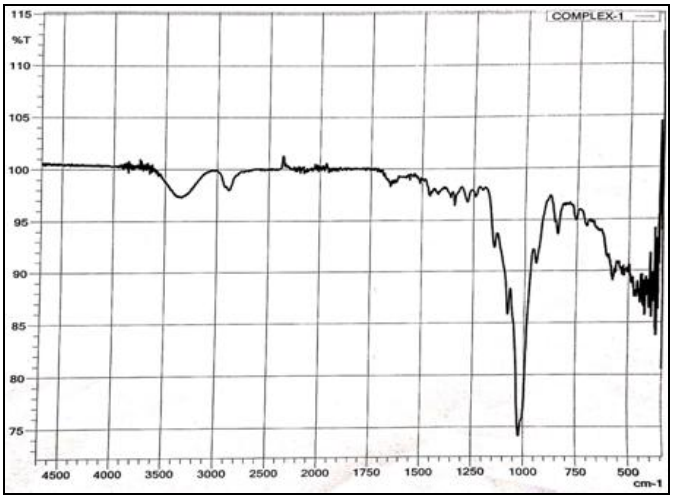

FIG. 4: FTIR SPECTRA OF CUR-ITSD

Satisfactory *in-vitro* disintegration time was obtained with formulation F4. Hence F4 was considered to be the optimized formulation for further studies. Formulation F4 comprised of Cur-ITSD with curcumin: PVP K30: Syloid XPD in the ratio 1:2:2. The antibacterial study for Cur-ITSD against *Streptococcus aureus* using the disk diffusion method showed that the antibacterial activity of Cur-ITSD formulation F4 was significantly better than plain curcumin against *Streptococcus aureus* as seen in **Fig. 5.** with a zone of inhibition 7.833 ± 0.288 mm.

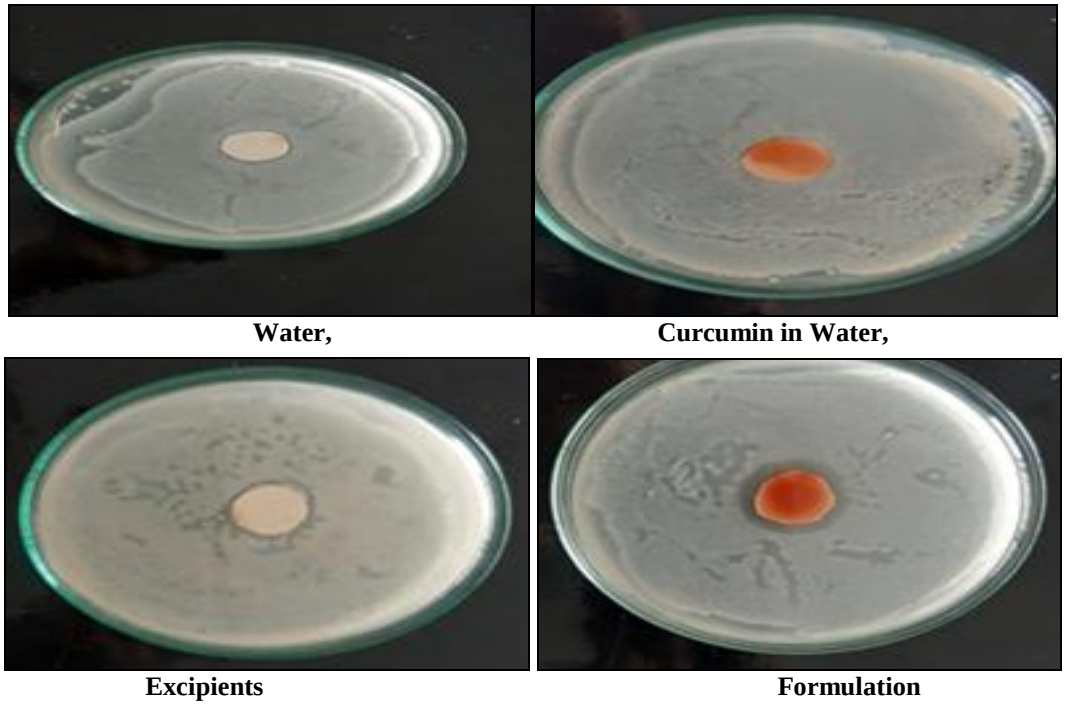

FIG. 5: EVALUATION OF ANTIBACTERIAL STUDY

Comparative dissolution profiles of plain curcumin lozenges, Cur-ITSD lozenge formulation F4 and marketed product is shown in **Fig. 6.** Formulation F4 provides a better and rapid dissolution rate comparable with that of the marketed product as depicted in **Table 3** and **Fig. 6.** The faster release in formulation F4 is attributed to the solid dispersion prepared using PVP K30 and Syloid XDP. Plain curcumin exhibits a poor dissolution rate because of its hydrophobic nature, and therefore, curcumin floats on the surface of the dissolution medium. The enhanced solubility and dissolution rate of Cur-ITSD is due to the combined effects of PVP K30 and Syloid XDP. Both these drug carriers contributed to improving the wettability of curcumin that increased drug dispersion in the dissolution medium, effectively reduced the surface tension between the drug and dissolution medium, and increased the effective surface area of the drug in solid dispersion.

TABLE 3: COMPARISON OF OPTIMIZED FORMULATION F4 AND MARKETED PRODUCT

Parameters	Optimized formulation F4	Marketed Product
Drug content (%)	98.9373 ± 0.0360	98.73± 0.750
In-vitro disintegration time (mins)	21.266 ± 1.105	30.1 ± 0.360
In-vitro drug release	$t_{50\%}$ (mins): 5.38 $t_{90\%}$ (mins): 494.47	$t_{50\%}$ (mins): 4.85 $t_{90\%}$ (mins): 432.90

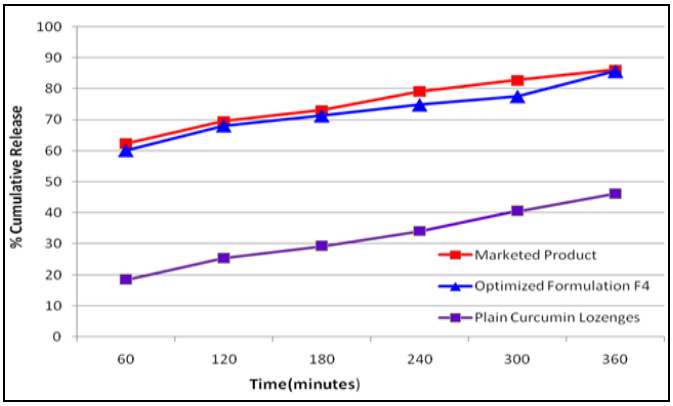

FIG. 6: DISSOLUTION PROFILES OF PLAIN CURCUMIN LOZENGES, OPTIMIZED FORMULATION F4, AND MARKETED PRODUCT

CONCLUSION: Hydrophilic polymer PVP K30 and water-insoluble surface modifying carrier Syloid XDP together contributed effectively in increasing solubility and dissolution rate of poorly water-soluble curcumin. Internal ternary solid dispersion of curcumin prepared using these two drug carriers improved its surface wettability, solubilizing effect and dissolution rate as compared to plain curcumin. The optimized lozenge formulation of curcumin prepared using internal ternary solid dispersion technique showed effective antibacterial activity and rapid drug release with prolonged action. It therefore can be a promising alternative to the marketed product as an immunity booster, anti-inflammatory and for oral hygiene.

CONFLICTS OF INTEREST: There is no conflict of interest.

ACKNOWLEDGMENT: The authors thank the management of Oriental College of Pharmacy for extending their support and co-operation throughout the research work. We also thank Konark Herbals Ltd. for providing gift samples of Curcumin; Gangwal Chemicals Pvt. Ltd. for providing gift samples of Sucrex and F-Melt C; Grace Davison Chemicals India Pvt. Ltd. for providing gift sample of Syloid® XDP; BASF for providing gift sample of Plasdone® K-30.

REFERENCES:

1. Hu L and Shi Y: Enhancement of oral bioavailability of curcumin by a novel solid dispersion system. AAPS Pharm Sci Tech 2015; 16(6): 1327-34.
2. López-Lázaro M: Anticancer and carcinogenic properties of curcumin: considerations for its clinical development as a cancer chemopreventive and chemotherapeutic agent. mol nutr food res 2008; 52: s103-27.
3. John M and Xie H: development and Pharmacokinetic Evaluation of a Curcumin Co-Solvent Formulation. Anticancer Res 2013; 33(10): 4285-91.
4. Yoysungnoen P and Wirachwong P: Anticancer and antiangiogenic effects of curcumin and tetrahydrocurcumin on implanted hepatocellular carcinoma in nude mice. World J Gastroenterol 2008; 14(13): 2003-09.
5. Modasiya M and Patel V: Studies on solubility of curcumin. Int J of Pharm & Life Sci 2012; 3(3): 1490-97.
6. Kapoor L: Handbook of ayurvedic medicinal plants. CRC Press Boca Raton Florida 1990; 185.
7. Kamran M and Shna R: Anticancer potential of curcumin: preclinical and clinical studies. BM Cancer 2020; 20(791): 1-11.
8. Kiuchi F and Goto Y: Nemotodial activity of turmeric. Chem Pharm Bull Tokyo 1993; 41(a): 1640-43.
9. Michele D and Riccardo G: Dietary curcumin: correlation between bioavailability and health potential. Nutrients 2019; 11(19): 2147.
10. Sabrina B and Marcos L: Improving the bioavailability of curcumin: is micro/nanoencapsulation the key. Therapeutic Delivery 2019; 10(2): 83-86.
11. Michaela S and Tereza Š: Preparation of solid dispersions with respect to the dissolution rate of active substance. Journal of Drug Delivery Science and Technology 2020; 56A: 101518.
12. Sultan A and Afzal H: Potential of solid dispersions to enhance solubility, bioavailability, and therapeutic efficacy of poorly water-soluble Drugs: newer formulation techniques, current marketed scenario and patents. Drug Delivery 2020; 27(1): 1625-43.
13. Phuong H and Thao T: Nano-sized solid dispersions for improving the bioavailability of poorly water-soluble drugs. Current Pharma Design 2020; 26(38): 4917-24.
14. Tuan-Tu L and Abdul K: Delivery of poorly soluble drugs via mesoporous silica: impact of drug overloading on release and thermal profiles. Powder Tech 2019; 11(2): 1-16.
15. Laura J and John P: Enhancing the dissolution of phenylbutazone using Syloid® based mesoporous silicas for oral equine applications. Journal of Pharmaceutical Analysis 2018; 8(3): 181-86.

How to cite this article:
Shanbhag PP, Lande S and Shaikh S: Studies on solid dispersion of curcumin using hydrophilic polymer with syloid xdp and lozenge characterization. Int J Pharm Sci & Res 2022; 13(3): 1338-43. doi: 10.13040/IJPSR.0975-8232.13(3).1338-43.