Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 4, Suppl 5, 2012

Research Article

FORMULATION AND EVALUATION OF TERNARY SOLID DISPERSION OF CURCUMIN

G. ARUN[1], P. SHWETA[2], KJ. UPENDRA[3]

Department of Pharmaceutics, Chandigarh College of Pharmacy, Landran, Mohali, India. Email: arun.gupta@inbox.com

Received: 10 Aug 2012, Revised and Accepted: 22 Sep 2012

ABSTRACT

Curcumin has a number of therapeutic effects. Curcumin is relatively non-toxic and safe. In spite of high efficacy and safety, curcumin has not yet been approved as a therapeutic agent, due to the poor solubility and oral bioavailability. Aim of this work is to formulate and evaluate the ternary dispersion (Third Generation Solid Dispersion) of curcumin in order to enhance the dissolution rate by solvent evaporation method (coprecipitation method) with the use of Carrier &Poloxamer i.e. PVP K30 and Lutrol F127. Ternary solid dispersions avoid the drug recrystallization and thus enhance the dissolution rate than Binary solid dispersion. A ternary solid dispersion meets the above requirement to prepare the highly soluble curcumin preparation and comparatively cheaper product ever before.

Keywords: Curcumin, Ternary dispersion, PVP K30, Lutrol, *In-vitro* dissolution study, XRD, DSC.

INTRODUCTION

Turmeric has been used in Asia for thousands of years in food, preservation of food, and as traditional medicine *(Aggarwal et al., 2007).* It is the yellow spice derived from the roots, rhizome, of the plant *Curcuma longa*. The curcuminoids which constitute approximately 5% of most turmeric preparations are a mixture of three principal compounds: curcumin (sometimes referred to as curcumin I), demethoxycurcumin (curcumin II), and bisdemethoxycurcumin (curcumin III). The majority of commercially available curcumin contains the following composition: curcumin I (77%), curcumin II (17%) and curcumin III (3%). *(Goel A et al , 2008)*

Extensive studies carried out by researchers around the globe have clearly demonstrated curcumin's great potential as a thercurcuminapeutic agent, and have paved the way towards conducting clinical trials for a variety of diseases including cancer, cardiovascular, neurological and gastrointestinal disorders, multiple sclerosis, diabetes type II, skin diseases, cystic fibrosis, cataract etc.Extensive investigation over the last five decades has indicated that curcumin reduces blood cholesterol, prevents LDL oxidation, inhibits platelet aggregation, suppresses thrombosis and myocardial infarction (MI), suppresses symptoms associated with type II, rheumatoid arthritis, multiple sclerosis (MS), and Alzheimer's disease, inhibits human immunodeficiency virus (HIV) replication, enhances wound healing, protects from liver injury, increases bile secretion, protects from cataract formation, and protects from pulmonary toxicity and fibrosis, is an anti-leishmaniasis and an antiatherosclerotic.

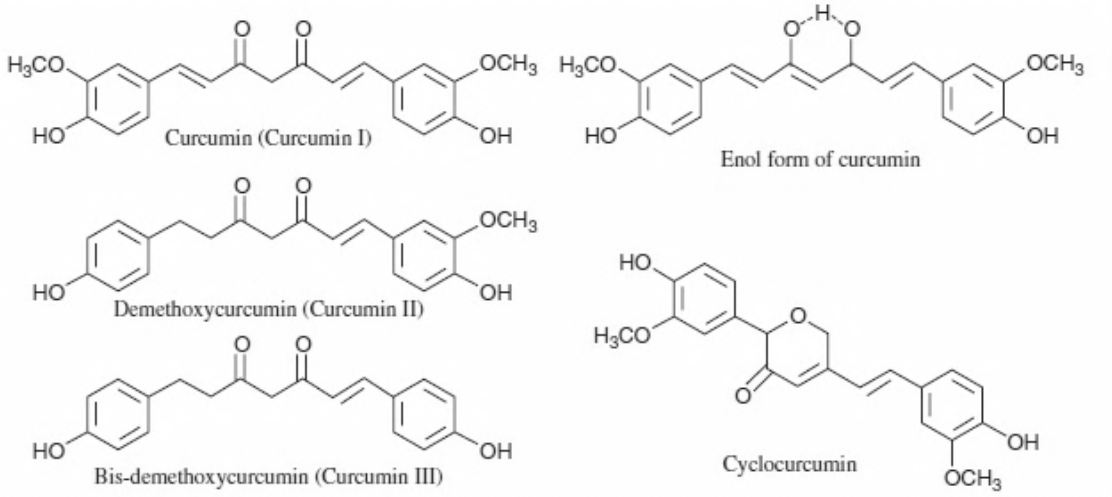


Fig. 1: Chemical structures of curcuminoids

Curcumin has a number of therapeutic agents; still it is not approved as a therapeutic agent due to its poor bioavailability and solubility. Thus development of formulation which enhances the solubility of curcumin is the main concern.

MATERIALS AND METHODS

Curcumin (Loba Chemicals),PVP K30 (Oswal Scientific store), Lutrol(Oswal Scientific store) and other ingredients used were of analytical grade. Double distilled water was used throughout the study.

Preparation of Ternary Dispersion of Curcumin

The first step in the solvent method is the preparation of a solution containing curcumin, polyvinylpyrrolidone and lutrol. The second step involves the removal of solvent i.e. Ethanol by rota evaporator resulting in formation of a solid dispersion. Then obtained particles were scrapped off and particles were finedin mortar pastel and sieving. Curcumin, PVP K30 and lutrol solid dispersions (SDs) in following ratios were prepared by solvent evaporation method in ethanol solution.

Table 1: Solid dispersions of curcumin

Formulation code	Curcumin	PVP K30	Lutrol
A1	1	1	1
A2	1	2	1
A3	1	4	1
A4	1	6	1
A5	1	8	1
A6	1	10	1
A7	1	8.5	1
A8	1	7.5	1

RESULT AND DISCUSSION

The solid dispersions showed improvement in **solubility** when compared to pure drug as well as Physical mixture. The results show that Curcumin solubility of ternary solid dispersion was affected by polymer content. The result shows that increase in the ratio of polymer up to an extent (1:8:1) improves solubility and above that there is decrease in the solubility. Dissolution efficiency was decreased at higher PVP K30 concentrations suggesting built up of viscosity in the diffusion layer around the dissolving particles that retarded further drug dissolution. Lutrol was able to enhance dissolution efficiency significantly due to the surface active property of Poloxamer. Result shows the maximum solubility of A5 formulation i.e. 60.61mcg/ml.The **drug content** of the prepared SD was found to be in the range of 91.42 and 92.53% indicating the applications of the present method for the preparation of SDs with good content uniformity. The drug content was found to be high in A5 and A8 formulations as compared to other formulations.**Dissolution study** was carried out with ternary solid dispersions and pure drug to find out their dissolution in the GIT. All the dispersions showed a good release rate when compared with pure curcumin. The rate improves when the ratio of PVP K30 increases up to an appropriate level. Formulations A5 showed the maximum release of 91.56 ± 2.14. Results of study are shown in following Table. It has been observed that the reaction rate is in the order of A5>A8>A7>A6>A4>A3>A2>A1. Thus the nonionic surfactants Lutrol and polymer PVP K30 increased the solubility and release rate of curcumin. The best ratios of curcumin, PVP K30 and Lutrol were ensured as 1:8:1 by dissolution rate of curcumin in vitro test.

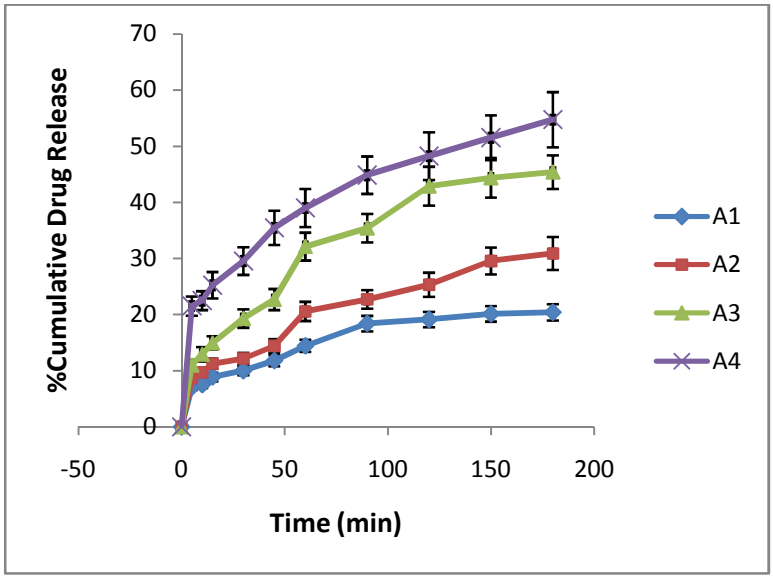


Fig. 2: *In-vitro* dissolution profile of Formulation A1, A2, A3 and A4

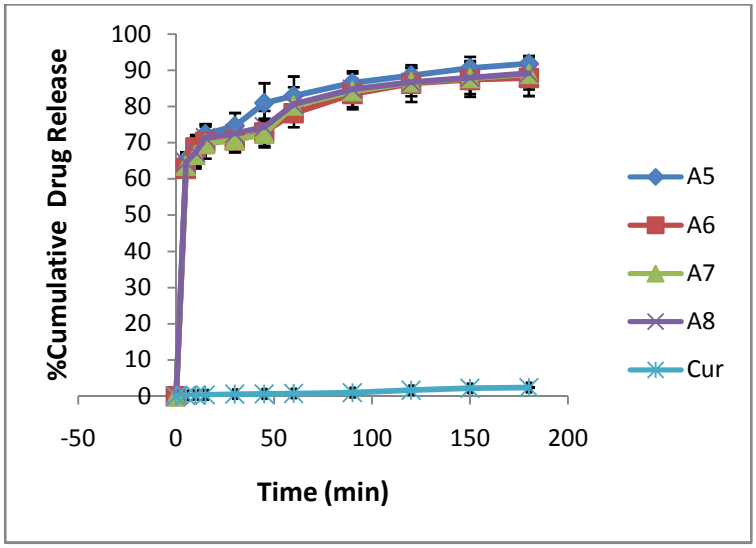


Fig. 3: *In-vitro* dissolution profile of Formulation A5, A6, A7, A8 and Pure Drug

Table 2: Percent Cumulative Drug Release (%CDR) of various formulation of curcumin dispersion

Time Min	Percent Cumulative Drug Release (%CDR)								
	A1	A2	A3	A4	A5	A6	A7	A8	Cur
0	0	0	0	0	0	0	0	0	0
5	7.09 ± 0.53	8.61 ± 0.62	11.02 ± 0.88	21.53 ± 1.71	40.48 ± 0.35	35.18 ± 0.7	39.08 ± 3.05	39.17 ± 2.64	0.18 ± 0.01
10	7.56 ± 0.66	9.67 ± 0.6	12.94 ± 1.29	22.49 ± 1.68	54.79 ± 0.72	49.71 ± 3.46	50.75 ± 3.19	50.81 ± 4.39	0.27 ± 0.01
15	8.90 ± 0.75	11.25 ± 0.91	14.96 ± 1.21	25.23 ± 2.36	64.28 ± 2.77	56.20 ± 4.69	57.85 ± 2.48	58.61 ± 3	0.32 ± 0.01
30	10.01 ± 0.78	12.15 ± 0.99	19.31 ± 1.65	29.55 ± 2.47	71.87 ± 3.57	62.98 ± 3.38	63.19 ± 3.22	63.44 ± 2.72	0.55 ± 0.026
45	11.8 ± 1.02	14.41 ± 1.23	22.68 ± 1.88	35.46 ± 3.04	80.67 ± 5.47	74.29 ± 3.75	74.78 ± 3.76	74.09 ± 4.38	0.58 ± 0.026
60	14.43 ± 1.08	20.57 ± 1.71	32.12 ± 2.48	38.99 ± 3.39	82.67 ± 5.32	77.75 ± 3.9	79.87 ± 3.71	80.51 ± 4.71	0.73 ± 0.026
90	18.40 ± 1.38	22.71 ± 1.64	35.40 ± 2.53	44.85 ± 3.34	86.24 ± 2.63	83.05 ± 4.18	83.65 ± 1.51	84.71 ± 4.96	0.97 ± 0.026
120	19.13 ± 1.37	25.33 ± 2.15	42.89 ± 3.46	48.23 ± 4.25	88.26 ± 2.12	85.94 ± 5.11	86.11 ± 2.45	86.67 ± 3.95	1.62 ± 0.06
150	20.12 ± 1.38	29.56 ± 2.38	44.37 ± 3.52	51.52 ± 3.98	90.29 ± 3.11	87.02 ± 4.76	87.25 ± 2.96	87.89 ± 4.59	2.16 ± 0.02
180	20.41 ± 1.45	30.89 ± 2.94	45.39 ± 3	54.73 ± 4.92	91.56 ± 2.14	87.48 ± 4.98	88.39 ± 2.89	89.11 ± 4.51	2.36 ± 0.08

In order to verify possible changes in the crystalline character of the drug, XRD analysis was made with pure curcumin, PVP K30, Lutrol, physical mixture, and dispersion. The physical mixture and curcumin show the same crystalline phases; however, in general, the peaks decreased in the dispersion diffractogram, indicating a decrease in curcumincrystallinity in the solid dispersion. XRD of pure curcumin showed sharp peaks. In SDs the characteristic peaks of drug disappeared and at higher proportions of PVP i.e. 1:8:1(A5), characteristic hump of amorphous form was observed.

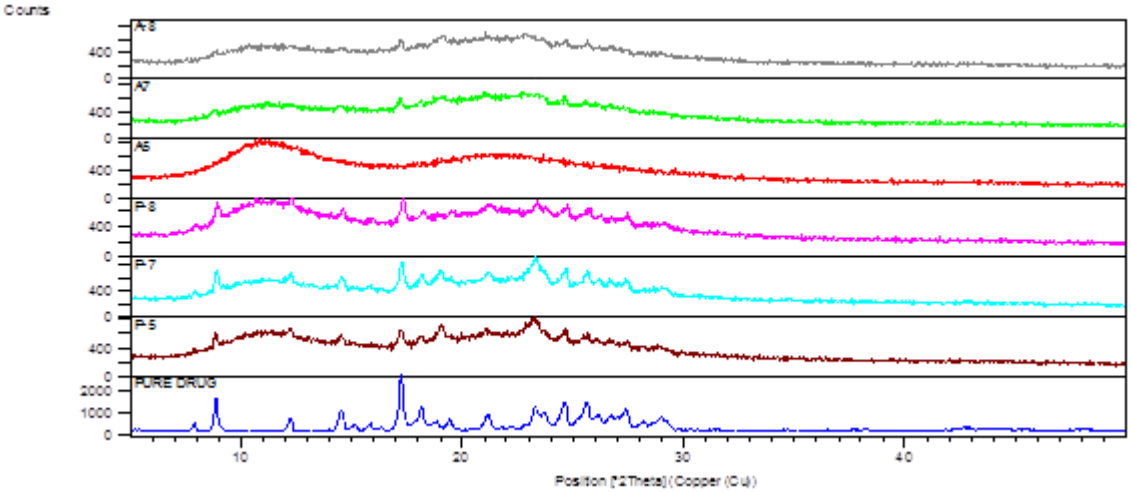


Fig. 4: XRD of SD, PM and Pure Drug

The IR Spectrographs of solid dispersions which indicted no interaction of curcumin with carriers. The chemical structure of curcumin showed the functional groups of phenolic OH, C=O and aromatic C=C which shows the peaks at 3500-3300 cm^{-1}, 1625 – 1640 cm^{-1} and 1520 – 1400 cm^{-1} in the IR spectrum. These peaks were observed in both pure drug & physical mixture as well as in solid dispersion indicating no interaction between drug and polymer.

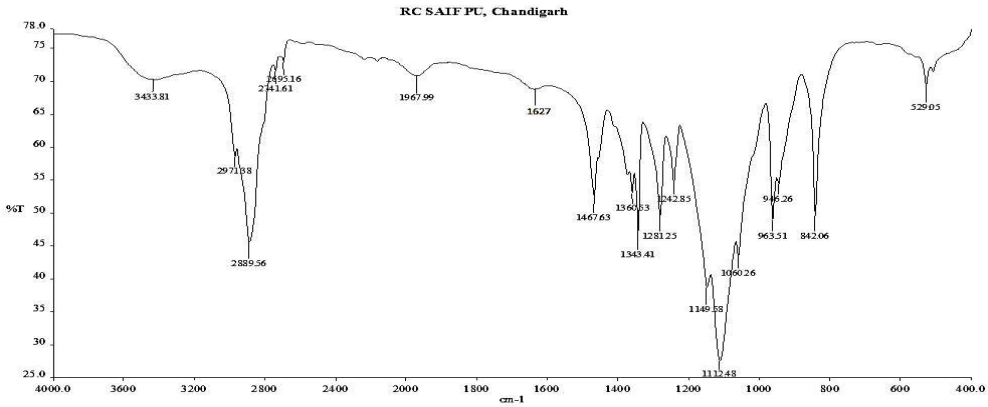


Fig. 5: FTIR spectra of Solid Dispersion of formulation A5

The morphology of the ternary dispersion was studied by SEM. SEM of curcumin exhibited flat broken needles of different sizes, with well-developed edges (Fig.6). Curcumin powder has a rectangular shape and that solid dispersion was spherical and porous agglomerates of smaller particles. Ternary Solid dispersion showed spherical particles, rough with pinholes. (Fig.7(a), (b)). Pure drug and A5 formulation are shown with magnifications of 1500 and 1000x in Figs.

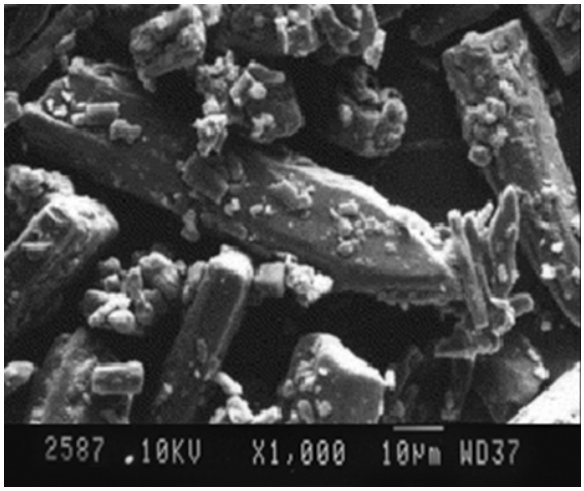
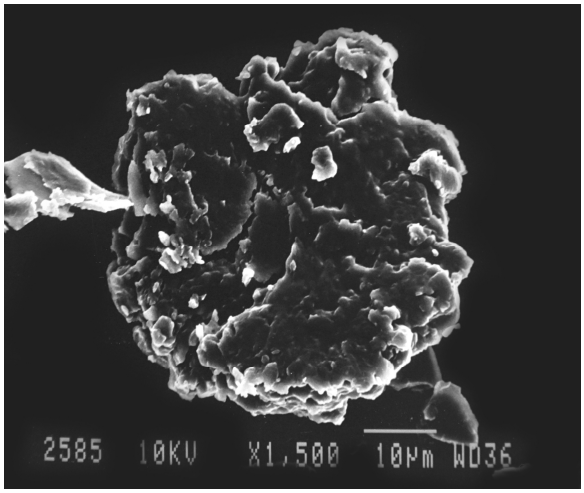


Fig. 6: SEM of pure curcumin



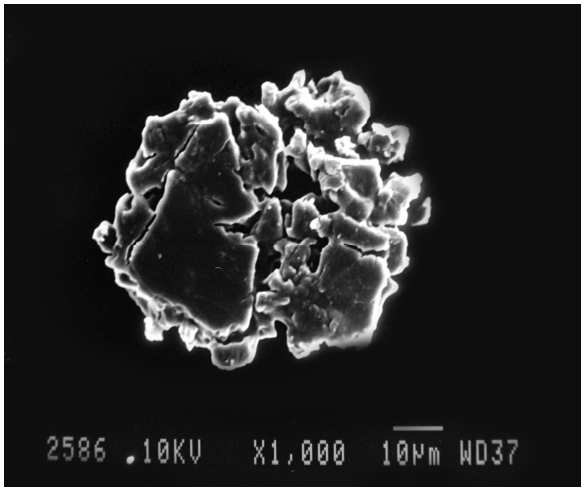


Fig. 7: Solid dispersion of curcumin:PVP:lutrol in the ratio of 1:8:1 (a and b)

DSC can indicate many changes in DS thermal properties, like the loss of moisture, melting, crystallization, glass transition, and chemical degradation. DSC was performed in order to verify the crystalline and amorphous nature of the drug. The thermograms shown in figure 8, 9, 10 shows sharp peaks at 179 ºC, 79 ºC, 60 ºC. These figures shows sharp melting point of curcumin, PVP K30 and Lutrol F127 respectively. So these sharp peaks indicate the crystalline nature of the pure drug, polymer and the poloxamer, where as in case of solid dispersion (Fig. 11), A5 formulation no sharp peak is observed which clearly indicates the amorphous nature of the formulation.

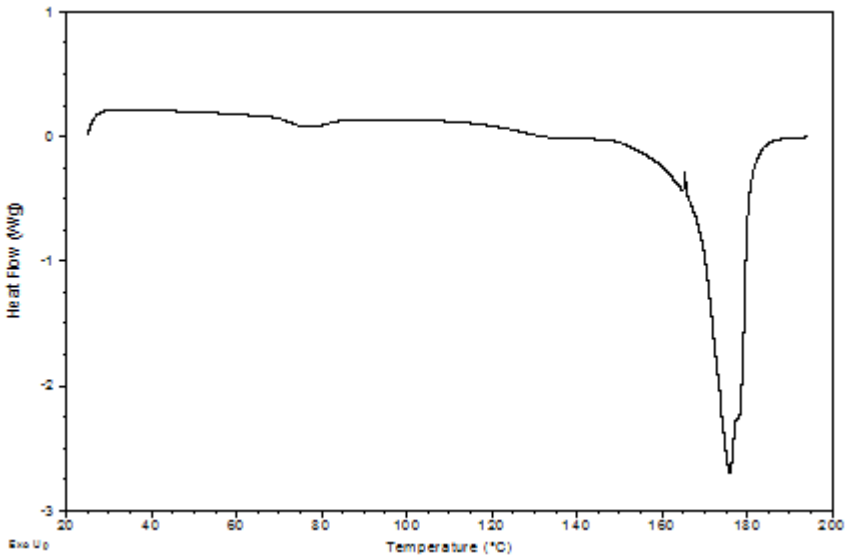


Fig. 8: DSC thermogramCurcumin

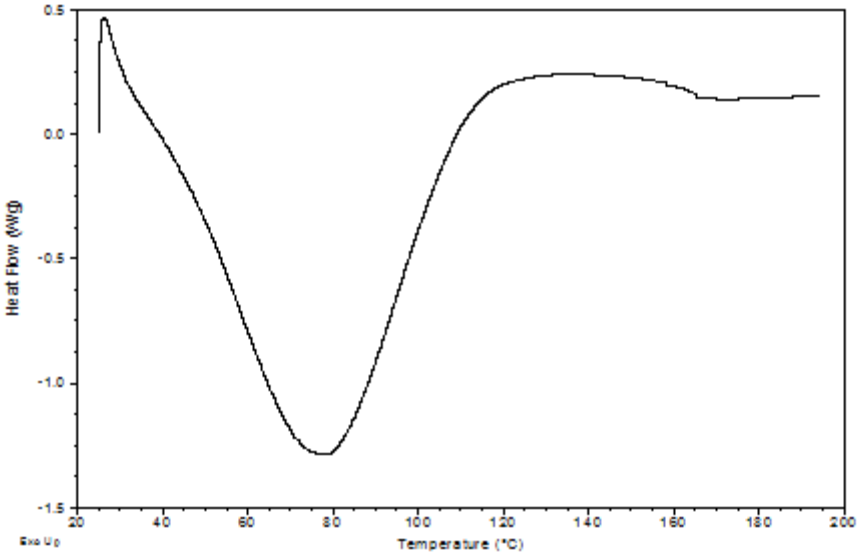


Fig. 9: DSC thermogram for PVP K30

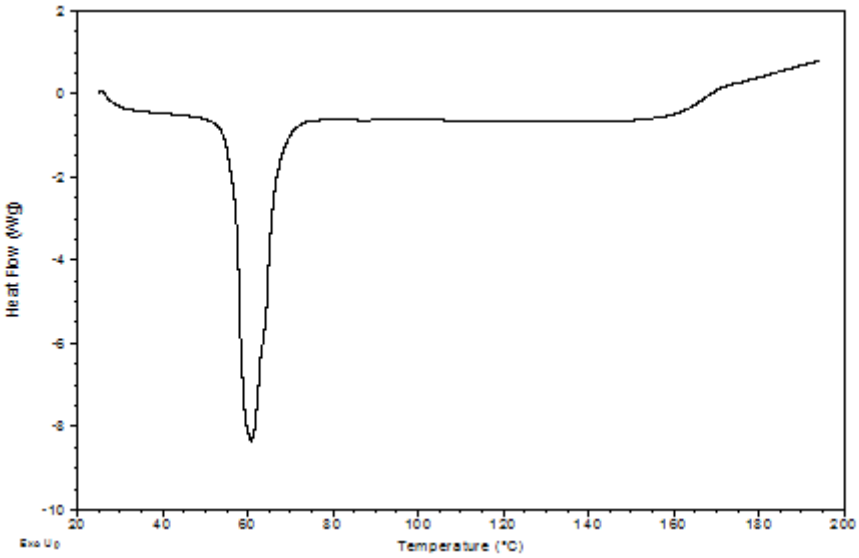


Fig. 10: DSC thermogram for Lutrol

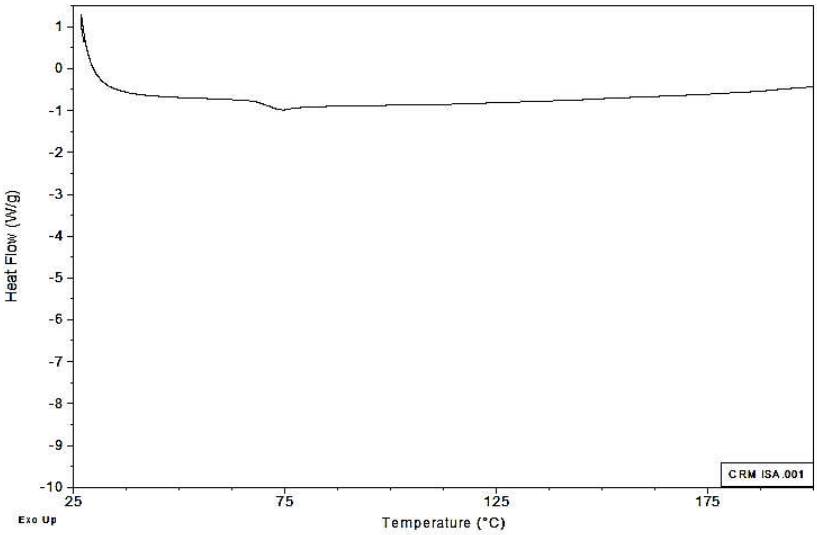


Fig. 11: DSC thermogram for A5 formulation

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