**INTERNATIONAL RESEARCH JOURNAL OF PHARMACY**

www.irjponline.com

ISSN 2230 – 8407

Research Article

# ASSESSMENT OF PHARMACOKINETIC PARAMETERS OF PHARMACODYNAMICALLY ACTIVE CURCUMIN GEL FOR ASSESSMENT OF CAUSE FOR COMPLETE RECOVERY OF RHEUMATOID ARTHRITIS

Jeevana Jyothi B *, Muni Raja lakshmi K

Institute of Pharmaceutical Technology, Sri Padmavati Mahila Viswavidyalayam (Women's University), Tirupati (A.P), India

*Corresponding Author Email: jeevanajyothib@yahoo.com

Article Received on: 02/08/17 Approved for publication: 03/09/17

**DOI: 10.7897/2230-8407.089156**

**ABSTRACT**

Curcumin gel prepared with solid lipid nanoparticles (SLN's) revealed its high *ex-vivo* characteristics and pharmacodynamically effective against collagen induced rheumatoid arthritis (RA) for rats. Hence the present research work was aimed to assess the reason for complete disappearance of swellings appeared due to RA. Therefore, pharmacokinetic parameters were estimated by self-developed HPLC method of analysis. Two groups were treated with topically applied gels. One group with curcumin gel made with SLN's and other group with gel containing pure curcumin. Pharmacokinetic parameters of gel with SLN's of curcumin were found to be $C_{max}$, $t_{1/2}$, and $AUC_{0-t}$ 18.95 µg/ml, 5.833 hours and 416.75 µg/ml/hour respectively and $C_{max}$, $t_{1/2}$, and $AUC_{0-t}$ of pure curcumin gel were found be 8.786 µg/ml, 4.9691 hours and 253.6 mg/ml/hour respectively. $T_{max}$ for both formulations was found to be 2.018 hours and 2.6492 hours respectively. The amount of drug absorbed is higher with the gel containing SLN's of curcumin ($C_{max}$ = 18.95 µg/ml) compared to pure curcumin gel ($C_{max}$ = 8.786 µg/ml). It also shows that gel containing SLN's of curcumin which has regression value of 0.973 when compared with ***ex-vivo*** permeation studies. Hence the gel exhibits maximum accumulation of drug at site of action like swollen joints as well as reasonable percent availability of curcumin in blood plasma leading to effective recovery of rheumatoid arthritis.

**Keywords:** Gel containing Curcumin SLN's, gel containing pure curcumin, pharmacokinetic parameters

## INTRODUCTION

NSAIDs used orally for treatment of rheumatoid arthritis possess side effects and at this context cutaneous drug delivery of both lipophilic and hydrophilic drugs can be possible without side effects by novel drug delivery formulations such as nanoparticles, solid lipid nanoparticles, liposomes etc,.[1, 2.]

In rheumatoid arthritis treatment can be accomplished through skin with topical formulations. The drug molecules applied on the skin surface is always possible to transport through the skin and reaches systemic circulation. The presence of excipients allows the entry of drug molecules in the deeper skin and thus enters in to systemic circulation[3]. The amount of drug entered in to systemic circulation can be assessed by pharmacokinetic parameters

The aim of the present study is to assess pharmacokinetic parameters of gel containing SLN's of curcumin upon application at the swollen hind paws of collagen induced rheumatoid arthritis rats that exhibited pharmacodynamic effect or treatment of RA as targeted drug delivery system.

## MATERIALS AND METHODS

Curcumin and stearic acid was purchased from Molychem, India. Potassium dihydrogen phosphate, sodium hydroxide, acetonitrile HPLC grade and methanol HPLC grade were purchased from Hi media, INDIA. Poloxomer 188 was purchased from Hi media, India. Carbopol and Sodium Carboxy Methyl Cellulose were purchased from SD fine chemicals Ltd.

### Step 1: Preparation of solid lipid nanoparticles of curcumin

Solid lipid nanoparticles of curcumin were prepared by solvent injection method using curcumin (500 mg), stearic acid (750 mg) and poloxomer 188 (6%). Percentage of drug release for these nanoparticles was 89.17% in 8 hours and it was converted to gel[4].

### Step 2: Preparation of Curcumin gel with solid lipid nanoparticles

Curcumin gel with solid lipid nanoparticles was prepared by using SLN's equivalent to contain 500 mg of curcumin, carbopol 934: Na CMC (1:3). For the purpose of comparison another curcumin gel was prepared using 500 mg of pure curcumin, carbopol 934: Na CMC (1:3). ***Ex-vivo*** permeation studies of gel containing SLN's of curcumin revealed drug diffusion of 96.39% and gel containing pure curcumin has drug diffusion of 27.04% in 2 hours[4]. These two formulations were estimated for pharmacokinetic parameters.

### Step 3: Pharmacokinetic parameters estimation of curcumin gel with solid lipid nanoparticles and gel made with pure curcumin using rat plasma by RP- HPLC method

Male wistar albino rats weighing around 200 gm to 250 gm were used for pharmacokinetic study. ***In-vivo*** studies were conducted for gels containing pure curcumin and solid lipid nanoparticles of curcumin. Gel equivalent to contain 110 mg/kg of rat weight was applied to collagen induced RA rats[5]. The studies were approved by Animal ethical committee, SPMVV. (Reg.no:

1677/PO/A/12//1AEC, May 2016). Two groups of rats each containing 6 for each of the formulation under study were used.

At predetermined time intervals, blood samples (0.2-0.3 ml) were collected from retro orbital plexus of rats in to eppendorf tubes containing 20% sodium citrate solution. The collected blood samples were coagulated by centrifugation at 15000 rpm for 15 mins. 100 µl of clear plasma was spiked with 0.15 µg/ml of celecoxib as internal standard (IS) and methanol was added to make the volume up to 1 ml (for denaturation and precipitation of plasma proteins). The tubes were tightly capped, vortexed for 10 min and centrifuged at 15000 rpm for 15 min. Then the supernatant clear sample was filtered through 0.45 µm Millipore filter paper and 25 µl of the supernatant liquid was injected using HPLC at the wavelength of 254 nm for detection of curcumin. The analytical column used was Hibar C18 (4.6 i.d. × 150 mm, 5 µm) column. The flow rate of the mobile phase was adjusted to 1.2 ml/min[6, 7, 8].

**Table 1: *In-vivo* bioavailability study between plasma concentration of gel containing SLN's of curcumin and pure curcumin gel**

| S.No | Time in hours | Plasma Conc. of gel containing SLN's of curcumin ±SD (µg/ml) | Plasma Conc. of pure Curcumin gel± SD (µg/ml) |
|---|---|---|---|
| 1. | 0 | 0 | 0 |
| 2. | 0.166 | 0.76 ±0.01 | 0.15±0.02 |
| 3. | 0.33 | 1.62±0.06 | 0.63±0.01 |
| 4. | 0.5 | 2.96±0.04 | 1.54±0.03 |
| 5. | 0.75 | 9.76±0.01 | 3.42±0.03 |
| 6. | 1 | 11.76±0.02 | 6.39±0.05 |
| 7. | 1.5 | 14.35±0.04 | 6.96±0.02 |
| 8. | 2 | 18.53±0.03 | 8.68±0.01 |
| 9. | 4 | 10.62±0.05 | 6.52±0.04 |
| 10. | 8 | 8.26±0.04 | 4.53±0.03 |
| 11. | 24 | 1.36±0.04 | 0.54±0.01 |

**Table 2: *In-vivo* Pharmacokinetic parameters**

| S.No | Pharmacokinetic parameter | Gel containing SLN's of curcumin | Pure curcumin gel |
|---|---|---|---|
| 1. | Elimination rate constant ($K_e$) | 0.0695 $hour^{-1}$ | 0.0633 $hour^{-1}$ |
| 2. | Elimination $t_{½}$ | 9.971 hours | 10.947 hours |
| 3. | Absorption rate constant ($K_a$) | 0.3434 $hour^{-1}$ | 0.1899 $hours^{-1}$ |
| 4. | $t_{1/2}$ | 5.833 hours | 4.969 hours |
| 5. | Volume of distribution | 2.110 | 4.8387 |
| 6. | $T_{max}$ | 2.018 hours | 2.6492 hours |
| 7. | $C_{max}$ | 18.95 µg/ml | 8.7869 µg /ml |
| 8. | $AUC_{0-t}$ | 416.75 µg/ml/hour | 253.6 mg/ml/hour |

**Table 3: *Ex-vivo* permeation studies and percent drug plasma concentration of gel containing SLN's of curcumin**

| S.No | Time (hours) | Percentage of drug diffused | Percentage of plasma concentration |
|---|---|---|---|
| 1 | 0 | 0 | 0 |
| 2 | 0.166 | 42.36±0.03 | 15.69±0.03 |
| 3 | 0.33 | 58.21±0.04 | 32.65±0.04 |
| 4 | 0.5 | 62.15±0.02 | 39.23±0.03 |
| 5 | 0.75 | 68.23±0.03 | 43.08±0.02 |
| 6 | 1 | 72.16±0.01 | 56.84±0.01 |
| 7 | 1.5 | 88.64±0.02 | 61.78±0.01 |
| 8 | 2 | 96.39±0.01 | 68.36±0.02 |

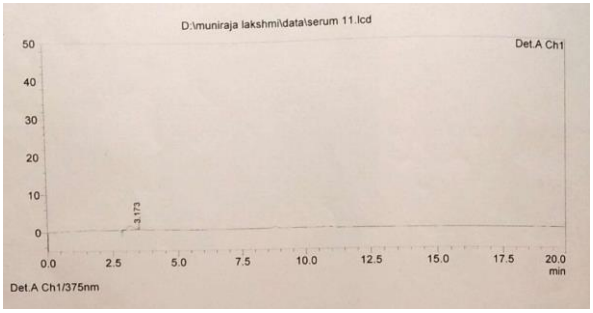


**Figure 1: HPLC chromatogram of plasma**

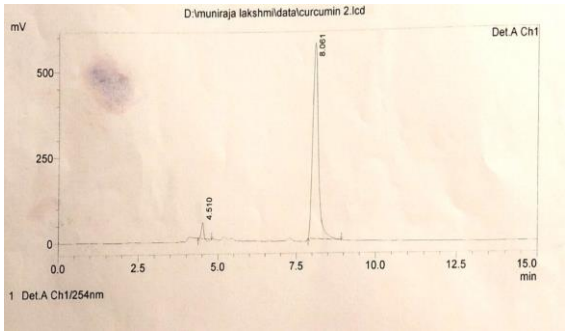


**Figure 2: HPLC chromatogram of curcumin and IS (Celecoxib) in mobile phase**

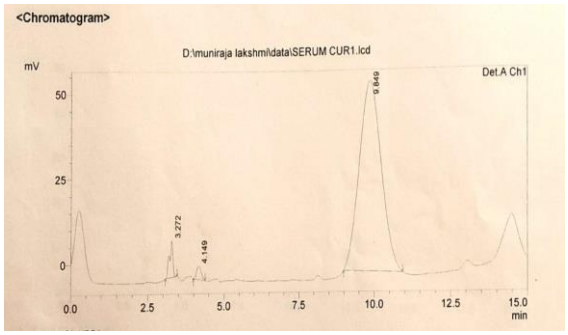


**Figure 3: HPLC chromatogram of IS (celecoxib) and curcumin in rat plasma**

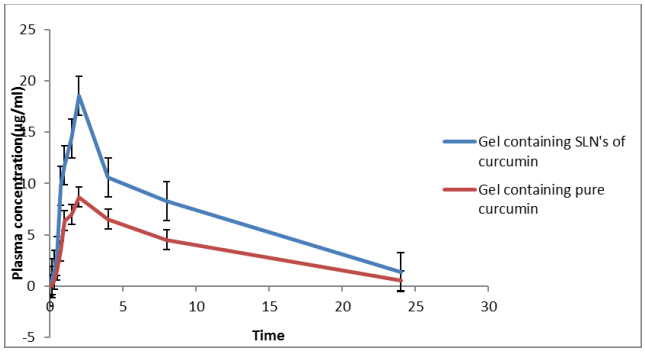


**Figure 4: In-*vivo* bioavailability study between plasma concentration of gel containing SLN's of curcumin and pure curcumin gel**

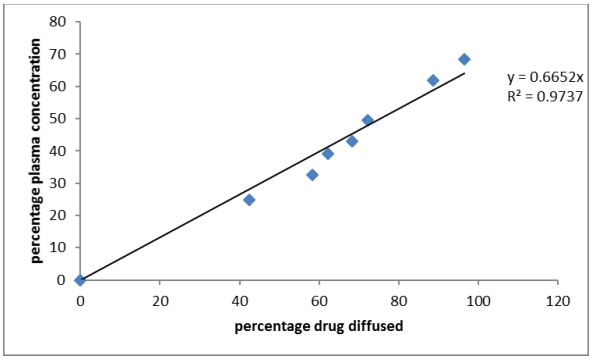


**Figure 5: IVIVC for gel containing SLN's of curcumin**

## RESULTS AND DISCUSSION

Plasma concentrations of curcumin after estimated by HPLC method from the two gels are shown in Table 1. Relevant chromatograms for plasma, curcumin and IS (celecoxib) are shown in Figure 1, 2 and 3.

Plasma concentration Vs. time graph was drawn and is shown in Figure 4. Pharmacokinetic parameters such as elimination rate constant ($K_e$), elimination t ½, absorption rate constant ($K_a$), $t_{½}$, volume of distribution, $t_{max}$, $C_{max}$, $AUC_{0-t}$ were estimated by exponential curve method. The curve was extrapolated and residual concentrations were calculated. The parameters calculated are given in the Table 2. $C_{max}$, $t_{1/2}$, and $AUC_{0-t}$ of gel containing curcumin SLN's was found to be 18.95 µg/ml, 5.833 hours and 416.75 µg/ml/hour respectively. Gel with pure curcumin evidenced $C_{max}$ of 8.786 µg/ml, $t_{1/2}$ as 4.9691 hours, and $AUC_{0-t}$ at 253.6 µg/ml/hour. It is observed that $T_{max}$ for two formulations was obtained with slight variation as 2.018 hours and 2.6492 hours. But the amount of drug absorbed is higher with the gel containing SLN's of curcumin ($C_{max}$ = 18.95 µg/ml) compared to pure curcumin gel ($C_{max}$ = 8.786 µg/ml).

From these studies it is concluded that pharmacokinetic parameters such as $C_{max}$ and $AUC_{0-t}$ are high for the curcumin gel prepared with solid lipid nanoparticles.

Hence the accumulation of curcumin after the application of gel with SLN's at the site of action obtained from *ex-vivo* permeation studies is compared with pharmacokinetic parameters.
The data of percent drug diffused Vs percent drug available in plasma is given in Table 3 and in Figure 5. Highest percent drug diffusion value was 96.39% whereas highest percent drug available in plasma was 68.36%. Due to this reasonable level accumulation of curcumin in plasma it is expected that the lesions and swelling on both hind paws were reduced in arthritis induced rats causing the total recovery from rheumatoid arthritis.

## ACKNOWLEDGEMENT

The authors sincerely acknowledge thanks to DST INSPIRE programme, New Delhi, INDIA for financial support.

## CONCLUSION

Curcumin gel prepared with solid lipid nanoparticles of curcumin exhibits maximum accumulation of drug at site of action like swollen joints as well as reasonable percent availability of curcumin in blood plasma hence leads to effective recovery of rheumatoid arthritis.

## REFERENCES

1. Shirish Ambulgekar, *In vitro* and *in vivo* investigation of topical formulations of erythromycin, *International Journal of Biopharmaceutics*. 2013; 4(2): 135-139.
2. Ying-Yue Wang, Chi-Tzong Hong, In vitro and in vivo evaluations of topically applied capsaicin and nonivamide from hydrogels, International Journal of Pharmaceutics 224 (2001) 89–104.
3. Kamal Dua, Kavita Pabreja, Aceclofenac topical dosage forms: *In vitro* and *in vivo* characterization, *Acta Pharm.* 60 (2010) 467–478
4. Jeevana Jyothi B, Muni raja Lakshmi K, Pharmacodynamic activity of curcumin gels produced from curcumin solid lipid nanoparticles for rheumatoid arthritis, International research journal of pharmacy, 2017, 8 (5), ISSN 2230 – 8407.

5. A.F. Zahidah, Curcumin as an Anti-Arthritic Agent in Collagen-Induced Arthritic *Sprague-Dawley* Rats, Sains Malaysiana 2012), 41(5), 591–595.
6. Vijay R Salunkhe, Snehal J Patil, UV spectrophotometric and hplc method development of quercetin and curcumin in polyherbal churna and its validation, International Journal of Pharmaceutical and Phytopharmacological Research, 2-16, ISSN 2249-6084
7. B. Jeevana Jyothi and T. Mounika, RP-HPLC Estimation of Cefpodoxime Proxetil in Rat Plasma, Asian Journal of Chemistry; Vol. 23, No. 3 (2011), 1186-1188.
8. Jeevana Jyothi B*, Guru Lakshmi. Gz, in-vitro and in vivo evaluation of transdermal prolonged release proniosomal gel formulations of propanolol HCl, International journal of drug development and research, 2014, Vol. 6, Issue 3, ISSN 0975-9344.

**Cite this article as:**

Jeevana Jyothi B and Muni Raja lakshmi K. Assessment of pharmacokinetic parameters of pharmacodynamically active curcumin gel for assessment of cause for complete recovery of Rheumatoid arthritis. Int. Res. J. Pharm. 2017;8(9):40-43 http://dx.doi.org/10.7897/2230-8407.089156

Source of support: DST INSPIRE programme, New Delhi, India, Conflict of interest: None Declared