

Formulation and Evaluation of Curcumin Microsponges and their Hepatoprotective Effect against Paracetamol-Induced Liver Toxicity in Rats

Gaurav N. Kasar^a, Khemchand R. Surana^{b*}, Pooja B. Rasal^c, Aman Upaganlawar^d, Manojkumar S. Mahajan^d, Sunil K. Mahajan^b

^a Department of Pharmacology, Vidya Amrut Dyan Pratishthan's, Vithai Pandit Deore Institute of Pharmacy, Shirsondi (Nashik), India – 423208.

^b Department of Pharmaceutical chemistry, Shreeshakti Shaikshanik Sanstha, Divine College of Pharmacy, Satana, Nashik, Affiliated to Savitribai Phule Pune University, Pune, Maharashtra 423301, India.

^c Department of Pharmacology, JES's SND College of Pharmacy, Babulgaon, Yeola, Nashik, India.

^d Department of Pharmacology, SNJB's Shriman Sureshdada Jain College of Pharmacy, Chandwad, Nashik, India.

Received: August 19, 2025 **Last Revision:** June 10, 2026 **Accepted:** August 03, 2026 **Available online:** October 13, 2026.

Abstract

Curcumin now has numerous pharmacological effects; however, its poor bioavailability limits its therapeutic potential. This study aimed to formulate curcumin microsponges and assess their effectiveness in shielding rat livers from paracetamol-induced damage. The toxicity was induced over a period of 10 days by administering 2 g/kg/day of paracetamol. Paracetamol severely damages the livers of rats by raising liver function markers such as ALT, AST, ALP, and total bilirubin levels while simultaneously lowering total protein levels. The mice received oral therapy for 10 days, including 100 mg/kg of curcumin microsponges and 100 mg/kg of plain curcumin (P-CUR). On the final day of the therapy, the rats were sacrificed, and the liver was excised for pathological analysis. Our findings indicate that microsponges exhibit a more potent hepatoprotective effect compared to conventional curcumin. Curcumin microsponges significantly reduced paracetamol-induced liver damage, as evidenced by a drop in liver function indicators. Our research indicates that curcumin microsponges may possess significant hepatoprotective properties.

Keywords: Microsponges; Paracetamol; Curcumin; Biomarkers; Liver; Hepatoprotective.

1. Introduction

The liver is among the most crucial organs and is primarily responsible for protein synthesis, detoxification, the generation of a variety of biochemical substances, and the control of the body's homeostasis [1].

It is constantly exposed to chemicals, alcohol and narcotics, which cause structural and functional alterations in the liver and lead to major complications, for example, hepatitis, cholestasis, hemochromatosis, and cirrhosis [2].

* Corresponding Author:

Khemchand R. Surana, Department of Pharmaceutical Chemistry, SSS's Divine College of Pharmacy, Nampur Road, Satana, Nashik, Maharashtra, India – 423301. E-mail: khemchandsurana772@gmail.com.

Cite this article as: Kasar G.N., Surana Kh.R., Rasal P.B., Upaganlawar A., Sonawane D.D., Mahajan S.K. Formulation and Evaluation of Curcumin Microsponges and their Hepatoprotective Effect against Paracetamol-Induced Liver Toxicity in Rats. Iran. J. Pharm. Sci., 2026, 22 (1): 391-403.

DOI: <https://doi.org/10.22037/ijps.v22i1.49935>

A common analgesic and antipyretic drug, paracetamol (PCM), is quite safe when used at prescribed dosages [3]. At a maximal dose of 4 g/day, PCM overdose may result in hepatotoxicity [4, 5]. Due to their enormous frequency, hepatic disorders are the main cause of illness and mortality worldwide. In excess, PCM can harm the liver by producing N-acetyl-p-benzoquinone imine (NAPQI), a toxic byproduct that is processed in the liver [6]. NAPQI interacts with hepatic proteins and glutathione, leading to lipid peroxidation, DNA breakage, free radical production, oxidative stress, and liver injury [7].

A wide range of ailments can be treated with several natural products [8]. The biologically active polyphenolic substance known as curcumin (CUR) originates from the plant *Curcuma longa* in the ginger family, *Zingiberaceae*. Reports revealed the protective effect of curcumin for the management of immune system illnesses [9], degenerative diseases of the brain [10], coronary artery diseases [11], respiratory failures [12], gastrointestinal diseases [13], inflammation and joint discomfort [14], anticancer [15], Antioxidant treatment and hepatoprotective characteristics [16]. CUR consumption promotes liver detoxification by altering GSH activity [17], which also reduces structural alteration of the liver. It showed ameliorative activity in the treatment of liver cancer, liver fibrosis, and cholestasis [18]. It has a wide range of molecular targets that can interact with, including those implicated in inflammation [19].

Curcumin's limited absorption and poor water solubility limit its application as a medication to treat ailments [20]. To improve the absorption and pharmacological activity of curcumin, a novel preparation is needed. In the present research, curcumin microsponges are used due to their greater effectiveness compared to natural curcumin [21]. Microsponges are highly stable, cross-linked, porous, and polymeric particles that range in size from 5 to 300 μm [22]. Because of their sponge-like appearance, microsponges exhibit unique compressibility and dissolution properties [23]. They exhibit fewer adverse reactions, are nontoxic, do not cause mutations, and have higher patient compliance [24].

Improving the dissolution rate and adhesive properties of the substances was the goal of the present

study. The microsponges were assessed using XRD, DSC, SEM, and FTIR techniques [25]. A surface examiner was used to evaluate the gel's mechanical strength inside the capsules, and the capsules were evaluated using a battery of pharmacological tests. The total drug content, manufacturing yield, average particle size, and entrapment efficiency were all calculated [26]. The effectiveness of the prepared microsponges was evaluated for their hepatoprotective activity in experimental animals by using a paracetamol-induced liver toxicity animal model [27].

The significance of the present study lies in addressing the major limitations associated with curcumin, including its poor aqueous solubility, rapid metabolism and low oral bioavailability, which restrict its therapeutic application despite its well-documented hepatoprotective potential. Microsponges represent a novel and promising drug delivery system capable of enhancing drug stability, controlling release kinetics and improving bioavailability. By formulating curcumin into microsphere-based delivery systems, the present research aims to enhance its hepatic retention and sustained therapeutic action. Furthermore, paracetamol-induced hepatotoxicity is a widely accepted experimental model that closely mimics drug-induced liver injury in humans. Therefore, this study is significant for demonstrating the dual advantages of formulation innovation and pharmacological evaluation, and for providing a potential strategy to improve the clinical efficacy of curcumin in the management of liver disorders.

2. Materials and Methods:

2.1. Drugs and chemicals:

Curcumin was obtained from Sudharshan Chemicals, Pune, India as a gift sample. Ethylcellulose and polyvinyl alcohol (PVA) were purchased from Loba Chemical Pvt. Ltd., Mumbai. The other chemicals utilized were of analytical grade.

2.2. Methods

2.2.1. Preparation of Microsponges

Oral microsponges are produced via quasi-emulsion solvent diffusion. This technique uses 1-4% w/v ethyl cellulose in dichloromethane as the internal phase. A Solution was incorporated by gradually adding the

medication (200 mg) to the ethyl cellulose solution while continuously mixing at 500 rpm. Subsequently, PVA (0.3%w/v) was added to the aqueous phase to create solution B (Table 1). To create a clear solution, sonicate both solutions on the probe for fifteen minutes. After that, stir continuously for two hours while adding solution A to solution B dropwise at 1000 rpm. Microsponges were stirred for 2 hours, after which they were filtered and dried in an air-fitted container in a hot-air oven [28].

2.2.2. Characterisation of Microsponges

2.2.2.1. Particle size analysis, zeta potential and PDI

Particle size analysis is used to determine the sizes of particles present in the sample. The curcumin formulation was subjected to particle size, zeta potential and Polydispersity index (PDI) by using HORIBA SCIENTIFIC SZ-100 [29].

2.2.2.2. Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR of the ethyl cellulose, curcumin, and curcumin microsponges sample was analysed using a Fourier transform infrared spectrophotometer (Bruker) over 400-4000 cm⁻¹, within the reported range [30].

2.2.2.3. Differential Scanning Calorimetry (DSC) Analysis

Differential scanning calorimetry (DSC) was performed to evaluate the thermal behaviour and possible interactions among curcumin, ethylcellulose, and curcumin-loaded microsponges. The analysis was performed using a differential scanning calorimeter (Q10, TA Instruments, USA). Prior to analysis, all

samples were thoroughly dried to remove residual moisture. Approximate weights of the powdered samples were placed in standard aluminium pans and hermetically sealed by crimping. The samples were then heated at a controlled rate of 10 °C/min over a temperature range of 30-400 °C under an inert nitrogen atmosphere, maintained at a flow rate of 100 ml/min to prevent oxidative degradation. An empty sealed aluminium pan was used as a reference. The resulting thermograms were recorded and analysed to determine melting transitions, thermal stability and possible changes in crystallinity or drug-polymer interactions [31].

2.2.3. Entrapment Efficiency

Take a weight of curcumin-loaded microsponges (10mg) dissolved in 10 mL methanol. Then centrifuge the solution and collect 1 mL of the supernatant. The solution is diluted with methanol, and absorbance is measured against a blank using a Shimadzu UV-1800 UV-visible spectrophotometer at 424 nm [32]. Moreover, the entrapment efficiency was calculated as follows:

Drug Entrapment Efficiency

$$= \frac{\text{Total Drug Conc.} - \text{Supernatant Drug Conc.}}{\text{Total Drug Conc.}} \times 100$$

2.2.4. Drug Loading Capacity

Drug loading capacity (DLC) is the amount of drug incorporated or entrapped within a carrier system relative to the total weight of the carrier or formulation. It is usually expressed as a percentage. Drug loading capacity indicates how much drug the delivery system can hold.

Table 1. Formulation of Curcumin Microsponges

Sr.No	Formulation	Curcumin (mg)	Ethyl cellulose (mg)	Polyvinyl alcohol (mg)	Dichloromethane (ml)	Distilled water (ml)
1.	F1	200	100	300	25	150
2.	F2	200	200	300	25	150
3.	F3	200	300	300	25	150
4.	F4	200	400	300	25	150
5.	F5	200	500	300	25	150

After dissolving the equivalent amount of curcumin (10 mg) in methanol (10 mL), weigh the curcumin-loaded microsponges, then dilute. We measured absorbance using a methanolic solution blank and a UV-visible spectrophotometer (Shimadzu UV-1800) set at 424 nm. We also used the following formulas to determine the medication loading efficiency [33].

$$\text{Drug Loading capacity} = \frac{M_{\text{act}}}{M_{\text{ms}}} \times 100$$

Where M_{act} is the actual weight of curcumin in curcumin microsponges, and M_{ms} is the weight quantity of microsponges powder.

Determining the drug-loading capacity of curcumin microsponges is necessary to confirm drug incorporation, optimise formulation parameters, and establish a direct relationship between the microsphere composition and the drug-release pattern. Finally, it is necessary to ensure the effectiveness and reliability of the microsphere-based drug delivery system.

2.2.5. Practical Yield

Practical Yield

$$= \frac{\text{Mass of Obtained microsponges}}{\text{Initial mass of polymer} + \text{Initial mass of polymer}} \times 100$$

2.2.6. Photomicroscopy

Photomicroscopy of curcumin microsponges was observed using an optical microscope. On the surface of the slide, an aqueous microsphere suspension drop was applied, covered with a cover slip, and observed under a 40X magnification lens [34].

2.2.7. Scanning Electron Microscopy (SEM)

The surface morphology of curcumin microsponges was studied using a scanning electron microscope to analyse the formulation [35].

2.2.8. X-ray Diffraction Studies

X-ray diffraction was used to determine crystalline and amorphous characteristics. Curcumin, ethylcellulose and curcumin microsponges were analysed using (LYNXYE XE T (1D mode): PSD counter) [36].

2.2.9. Stability Study

The stability of curcumin microsponges was assessed under accelerated conditions as per ICH Q1 guidelines. The preparation was placed in the stability chamber at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and $75\% \pm 5\%$ RH for 3 months. After the accelerated stability condition, microsponges were evaluated based on their physical appearance and an FTIR Study [37].

2.3. Hepatotoxicity study

2.3.1. Experimental Animals

Healthy adult Wistar rats of male sex, weighing 180–220 g, were used for the study. The animals were housed in polypropylene cages under standard laboratory conditions with a controlled temperature of $22 \pm 2^{\circ}\text{C}$, relative humidity of $55 \pm 5\%$ and a 12 h light/12 h dark cycle. The animals were provided with standard laboratory pellet diet and water ad libitum. All animals were acclimatised to laboratory conditions for at least 7 days prior to the commencement of the experiment. Four sets of six male Wistar rats each were prepared from healthy male rats. We purchased the rats from Wockhardt Ltd. in Aurangabad, India. The CCSEA's housing regulations were followed. The institution's IAEC approved the study's methodology (SSDJ/IAEC/2022-23/03).

2.4. Experimental Protocol

Rats were divided into four groups of six rats each. The 10-day course of treatment began on the first day [38, 39].

Group I:	Rats were treated with vehicle and served as the normal control.
Group II:	Rats were given paracetamol (2g/kg p.o. daily) for 10 days and considered as disease control.
Group III:	Rats were given a single daily oral dose of 2g/kg paracetamol and 100 mg/kg plain curcumin (P-CUR group) for 10 days, dissolved in 1% Tween 80.
Group IV:	Rats received a single daily dose of 2 g/kg paracetamol and curcumin microsponges (MS-CUR group), equivalent to 100 mg/kg curcumin orally, for 10 days, dissolved in 1% Tween 80.

Curcumin microsponges were given three hours after paracetamol was given. The treatment course lasted for ten days. On the last day of the protocol, blood was drawn from the retroorbital nerve using a microcapillary under ether anaesthesia, and the serum was separated using a high-speed centrifuge. Serum samples were used for various biochemical calculations and stored at -20°C. Following the cervical dislocation method of rat sacrifice, the liver was removed, washed in cold physiological saline, and preserved in 10% formalin solution for histological analysis. Using an assay kit (Clorol Clinical System Pvt Ltd., Uttarakhand), the serum levels of total protein, total bilirubin, AST, ALP, and ALT were determined.

2.5. Histopathological Examination

A piece of 5 µm was produced. Hematoxylin and eosin (H&E) staining was performed on the sections, and images were captured at the Optimus Diagnostic Laboratory in Nashik. A light microscope (400×) was used to examine the sections for general morphological changes [40].

2.6. Statistical Analysis

All variables were analysed using GraphPad Prism (version 5.0), and Dunnett's test was applied after ANOVA. Data were presented in terms of mean ± SEM (n=6). $p < 0.05$ was regarded as statistically significant for all variables evaluated.

3. Results and Discussion

3.1. Particle size analysis, zeta potential and PDI

The particle size of the curcumin microsponges formulation was measured using a zeta sizer, and the formulation ranged from 2.12 µm to 4.14 µm (**Table 2**).

This particle size is affected by the concentration of ethyl cellulose and magnetic stirrer speed. It was observed that increasing the polymer concentration and the formulation mixing speed increased the production yield and entrapment efficiency (F4 formulation), and that adding an excess amount of polymer to the formulation formed a cake. The F4 formulation shows good zeta potential and polydispersity index (**Figures 1 and 2**).

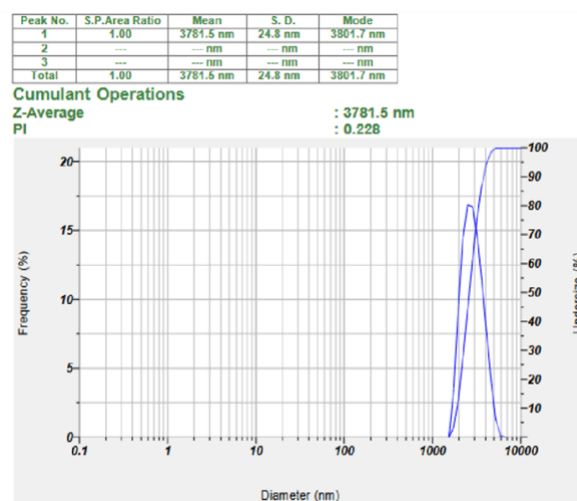


Figure 1. Particle size analysis and PDI of curcumin microsponges formulation

Zeta Potential (Mean) : -15.8 mV
Electrophoretic Mobility Mean : -0.000230 cm²/Vs

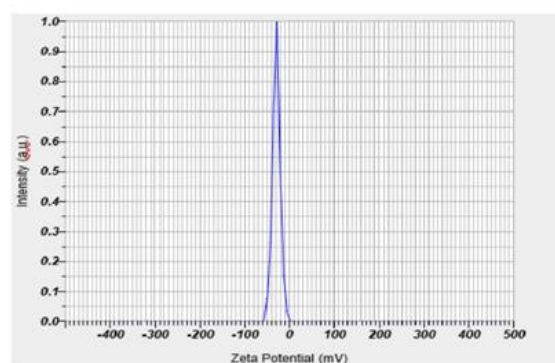


Figure 2. Zeta potential of curcumin microsponges formulation

Table 2. Particle size analysis.

Sr. No	Formulation code	Particle size (µm)	Entrapment efficiency (%)	Practical yield (%)	Drug loading capacity (%)
1.	F1	2.12	21.56	57	24.89
2.	F2	2.54	33	65	32.45
3.	F3	3.12	54.78	70	60.42
4.	F4	3.78	85	75	80.65
5.	F5	4.14	65.48	73	66.49

3.2. Fourier transform infrared spectroscopy (FTIR)

The FTIR spectra of curcumin, polyvinyl alcohol, ethylcellulose, and curcumin microsponges are shown in **Figure 3**. Curcumin's spectra in **Figure 3(a)** show a wide, sharp peak at 3504 cm^{-1} , which is the O-H stretch of the phenolic hydroxyl group. The aromatic ring vibrations have a peak at 1497 cm^{-1} , and the beta-diketone functional group has a C=O stretch at around 1618 cm^{-1} . The peak at 1269 cm^{-1} corresponds to the phenolic hydroxyl group C-O stretch. Peak 1036 cm^{-1} represents the aromatic rings C-H bend.

The curcumin microsponges formulation spectra in **Figure 3(b)** exhibit a large peak at around 3452 cm^{-1} , which is indicative of the O-H stretch formed by the hydroxyl groups of ethyl cellulose and the phenolic hydroxyl group of curcumin. A peak at 1603 cm^{-1} is the beta-diketone functional group of curcumin's C=O stretch. A peak located at 1732 cm^{-1} is indicative of the ester group's C=O stretch in ethyl cellulose. The aromatic ring vibrations of curcumin and the C-H bending vibrations of the ethyl cellulose backbone are represented by a series of peaks at 1541, 1510, and 1443. The C-O stretch of curcumin's phenolic hydroxyl group and the C-O-C stretch of the ethyl cellulose ether bond are represented by a peak at about 1241 cm^{-1} .

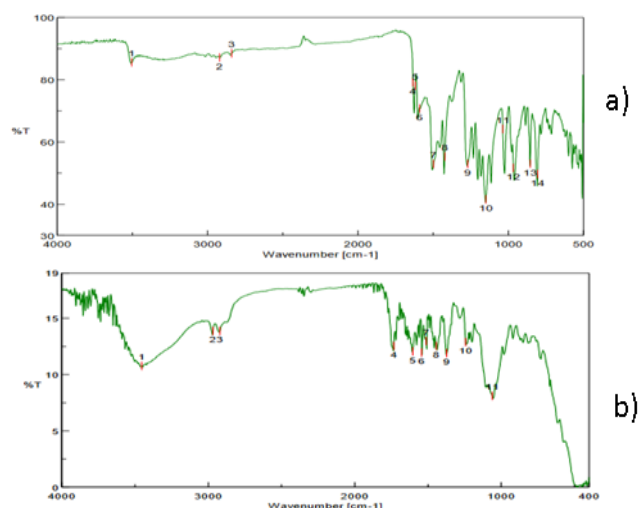


Figure 3. FTIP study of a) Curcumin, b) curcumin microsponges formulation

3.3. Differential Scanning Calorimetry Analysis (DSC):

Figure 4 shows, the DSC thermogram of curcumin, ethyl cellulose and curcumin microsponges. In **Figure 4(a)**, curcumin shows a sharp peak at 182.678°C, and ethyl cellulose, an amorphous substance, does not show a sharp endothermic peak, as shown in **Figure 4(b)**. Curcumin microsponges also show a sharp endothermic peak at 183.757°C. From this result, we concluded that our formulation is stable (**Figure 4c**).

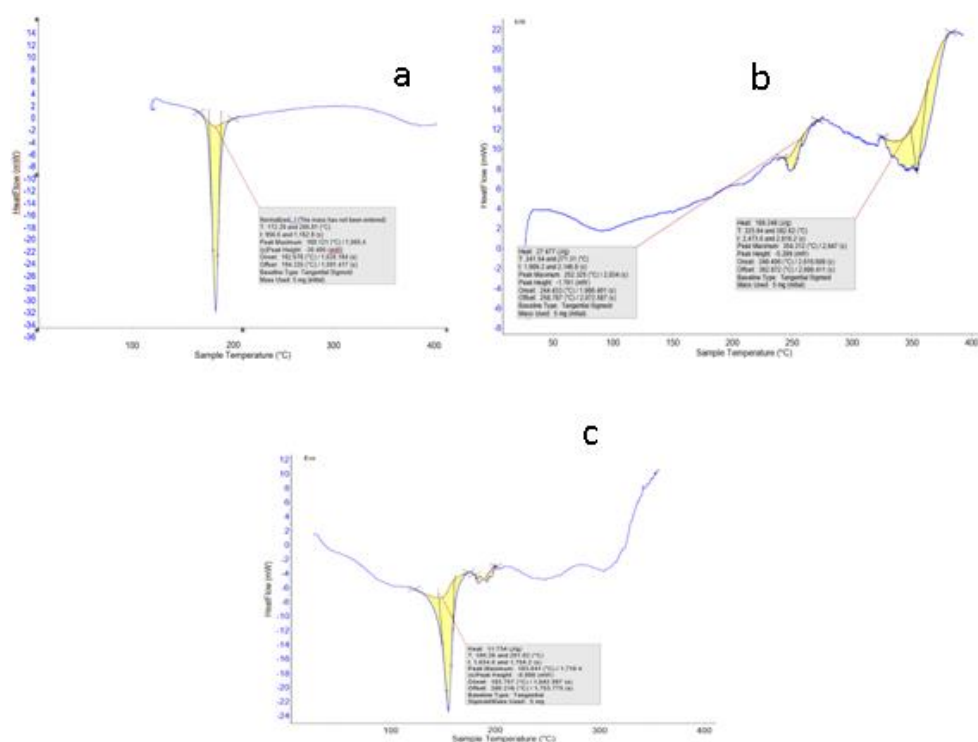


Figure 4. DSC curve a) Curcumin, b) Ethyl cellulose, c) Curcumin Microsponges

3.4. Entrapment Efficiency, Drug loading capacity and Practical yield

Table 3 displays the entrapment efficiency, drug loading capacity, and practical yield of different formulation batches of curcumin microsponges. The Entrapment efficiency value ranges between 21.56 and 85. The drug loading capacity of different formulations of curcumin varied between 24.89 and 80.65. Also, it shows the different practical yields of 57-75%. Particle size decreases with increasing formulation speed. The practical yield of the microsponges increases with increasing polymer content.

3.5. Photomicroscopy

Figure 5 shows the Photomicroscopy images of the curcumin microsponges. In these images, the microsponges appear spherical.

3.6. Scanning Electron Microscopy (SEM):

Figure 6 indicates the outer structure images obtained by SEM of curcumin microsponges. The images show that the microsponges are spherical, and no curcumin crystals are observed in these scanning electron microscopy images.

Table 3. Particle size analysis

Sr. No	Formulation code	Particle size (µm)	Entrapment efficiency (%)	Practical yield (%)	Drug loading capacity (%)
1.	F1	2.12	21.56	57	24.89
2.	F2	2.54	33	65	32.45
3.	F3	3.12	54.78	70	60.42
4.	F4	3.78	85	75	80.65
5.	F5	4.14	65.48	73	66.49

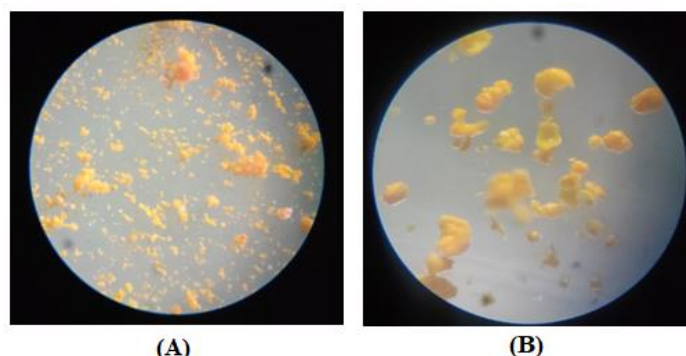


Figure 5: Photomicrographic images of formulated curcumin-loaded microsponges showing spherical morphology, surface characteristics and uniform particle distribution.

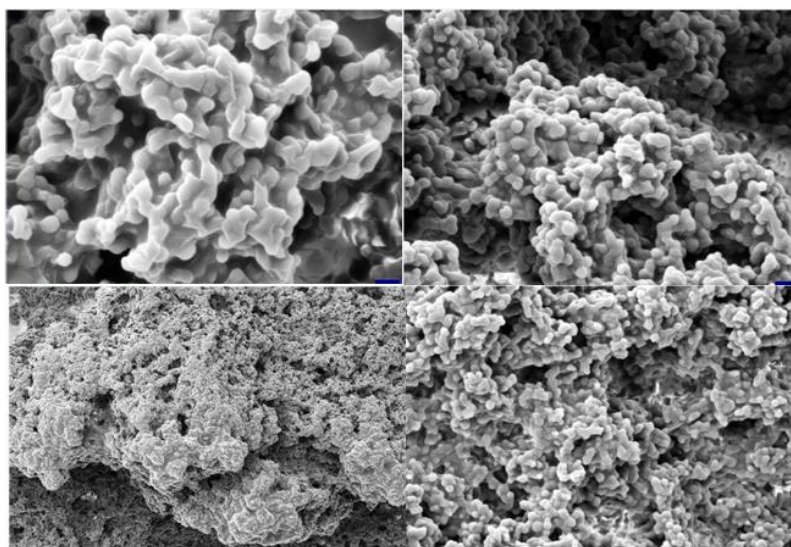


Figure 6. Scanning Electron Microscopy (SEM)

3.7. X-ray diffraction study

Figure 7 shows the X-ray diffraction spectra of ethyl cellulose, curcumin, and curcumin microsponges. The X-ray diffractogram of EC shows no distinct peaks, indicating it is amorphous. While the diffractogram of the curcumin microsponges exhibits strong peaks at 17°, 20°, 24°, and 28°, with reduced intensity, showing a decline in the crystalline character of the microsponges, which means the drug curcumin is encapsulated in the ethyl cellulose polymer., the spectra of curcumin show sharp peaks at 19°, 20°, 22°, and 25°, demonstrating the crystalline nature of curcumin.

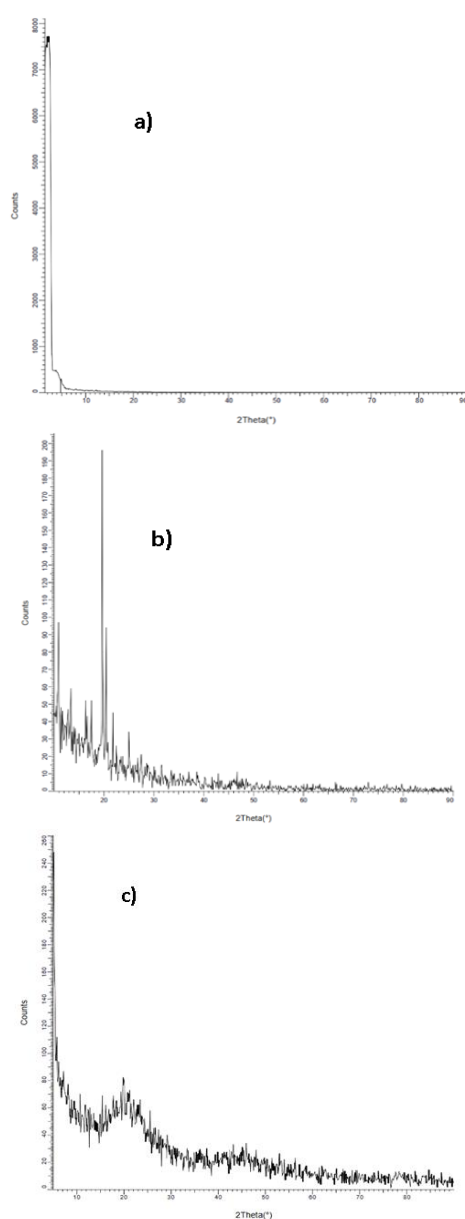


Figure 7. XRD for a) Ethyl cellulose b) Curcumin c) Curcumin Microsponges

3.8. Stability Study

The formulation F4 was subjected to a 3-month stability study under accelerated conditions and evaluated for physical appearance and FTIR spectroscopy. After 3 months of stability studies, the formulation shows no changes in appearance or in the FTIR spectrum. Additionally, the FTIR study shows that the formulation is stable. From these two parameters, it may be concluded that they have a good shelf life.

3.9. Effect of curcumin and curcumin microsponges on total protein in serum

Serum total protein was estimated as an indicator of hepatic synthetic function. Since the liver is responsible for the synthesis of major plasma proteins, any impairment due to paracetamol-induced hepatocellular damage results in reduced serum protein levels. Restoration of total protein levels following treatment reflects improvement in liver functional capacity. As shown in **Figure 8**, Rats treated with paracetamol only (Group II) displayed a marked decline ($p < 0.01$) in the serum level of total protein compared with normal rats. Rats administered curcumin alone showed an increase in total protein levels, but it was not significant. Whereas rats treated with curcumin microsponges showed a substantial ($p < 0.05$) increase in total protein levels compared to the sick group.

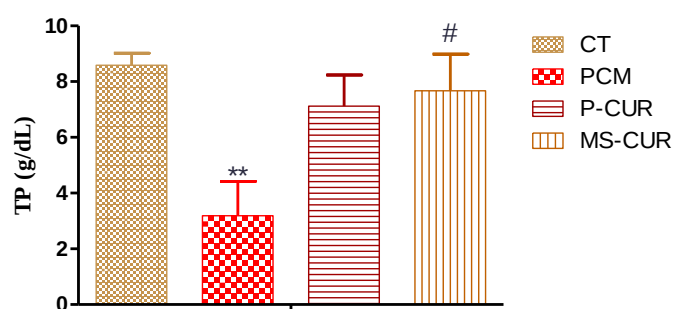


Figure 8. Effect of curcumin and curcumin microsponges on total protein in serum

Data were reported as mean $\pm$ SEM, $n=6$. ANOVA was applied with Dunnett's test for analysis. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared to normal and # $P < 0.05$, ## $P < 0.01$, ### $P < 0.001$ compared to PCM.

3.10. Effect of curcumin and curcumin microsponges on total bilirubin in serum

Compared with the control group, rats given paracetamol showed a significant ($p < 0.001$) increase in their blood total bilirubin levels. When rats were treated with curcumin after being inebriated with paracetamol, their blood total bilirubin levels decreased significantly ($p < 0.05$). Compared with the paracetamol group, rats treated with curcumin microsponges significantly ($p < 0.05$) reduced these levels (Figure 9).

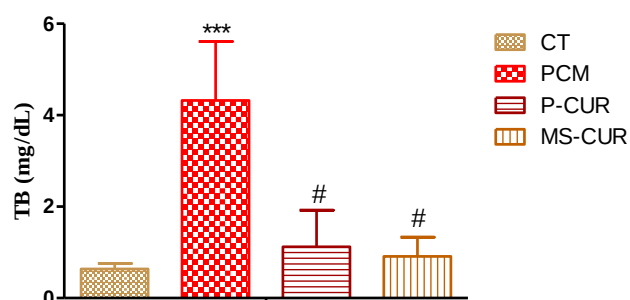


Figure 9. Effect of curcumin and curcumin microsponges on total bilirubin in serum

Data were reported as mean $\pm$ SEM, $n=6$. ANOVA was applied with Dunnett's test for analysis. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared to normal and # $P < 0.05$, ## $P < 0.01$, ### $P < 0.001$ compared to PCM.

3.11. Effect of curcumin and curcumin microsponges on liver enzyme activities in paracetamol-treated rats in serum

The level of liver enzyme activities in serum was monitored in all groups. Significant changes were observed in serum ALT, AST, and ALP activities in the diseased group compared with the normal group (Figure 10). Administration of curcumin to diseased rats displayed a significant ($p < 0.01$) decline in the level of liver activities. Whereas rats administered curcumin microsponges displayed ($p < 0.01$) powerful hepatoprotective activity by reducing levels of ALT, AST, and ALP compared with diseased paracetamol groups.

3.12. Histopathological Examination

Histopathological investigation is done as shown in Figure 11,

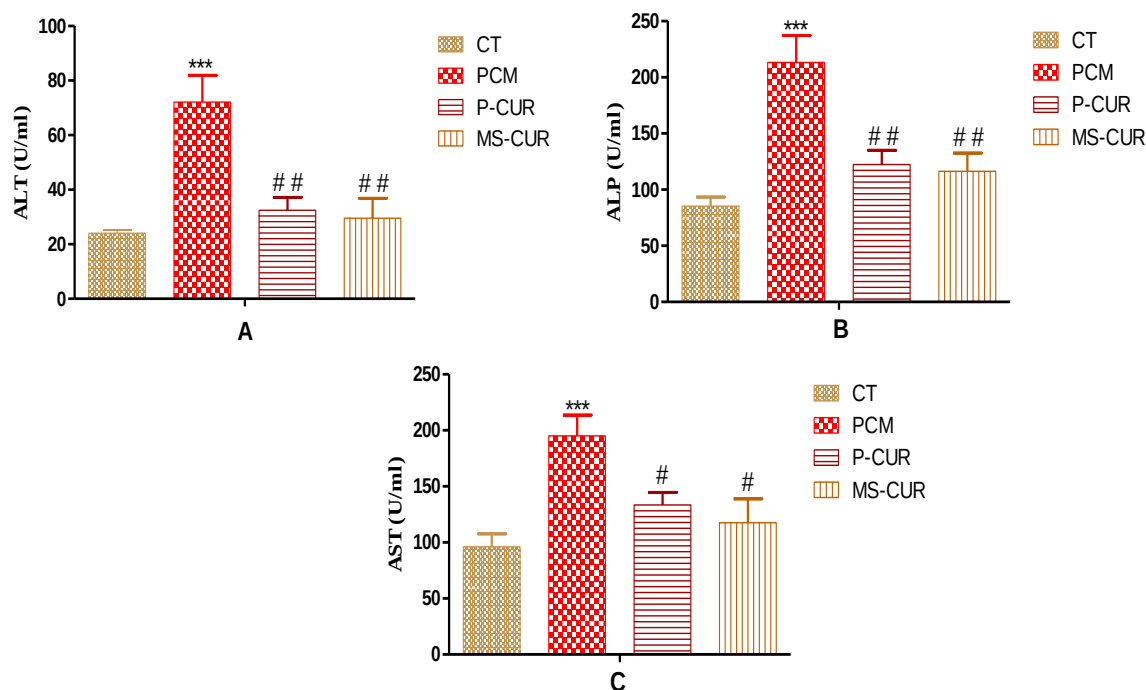


Figure 10. Effect of curcumin and curcumin microsponges on liver enzyme activities A) ALT, B) ALP and C) AST on paracetamol-treated rats in serum

Data was mentioned in terms of mean $\pm$ SEM $n=6$. ANOVA was applied with Dunnett's t test for analysis. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared to normal and # $P < 0.05$, ## $P < 0.01$, ### $P < 0.001$ compared to PCM.

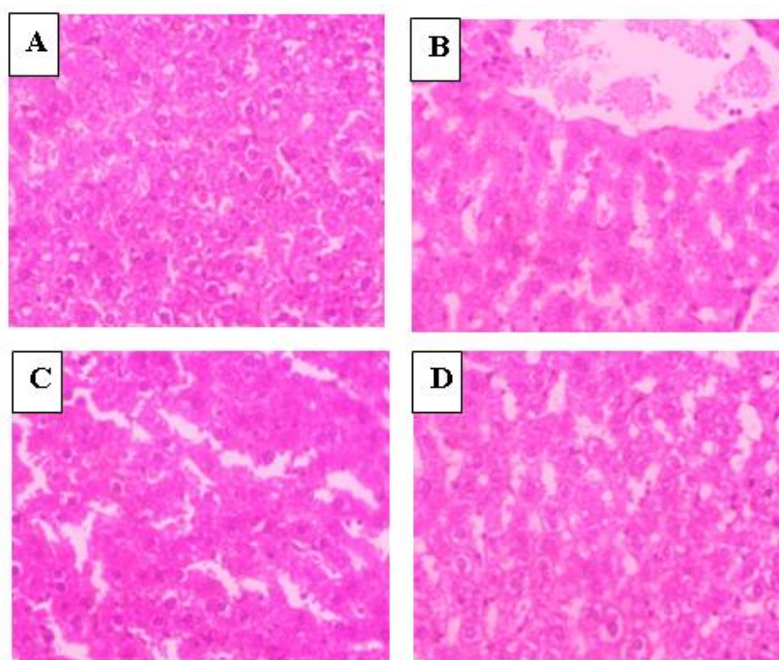


Figure 11. Histopathological analysis after PCM overdose and treatment with P-CUR or MS-CUR (H & E, 400) in the rat livers

3.13. Discussion

Clinicians face significant challenges in treating drug-related liver injuries, given their prevalence as a cause of liver failure. The most well-known, mechanistically well-studied, and clinically applicable model is the PCM-induced hepatotoxicity model. Numerous studies have utilised paracetamol to cause liver injury. Oxidative stress, inflammation, and cell death pathways all contribute to paracetamol's toxicity in the liver. Several therapeutic approaches, including the use of organic substances like curcumin, have been researched to reduce the liver damage caused by paracetamol.

The development of novel formulations for curcumin delivery is crucial given its numerous positive effects. According to studies, curcumin can neutralise reactive oxygen species, prevent lipid peroxidation, and alter various signalling pathways involved in liver damage. Due to its limited solubility, curcumin has poor absorption. In this study, we successfully formulated curcumin microsponges that enhance the compound's bioavailability. The benefits of using microsponges as a drug delivery system include prolonged curcumin release and increased bioavailability, which may improve its efficacy in treating liver toxicity.

Rahman *et al.* (2025) aimed to assess the potential effects of curcumin and paracetamol on maternal Wistar

rats and their fetuses during gestation. Curcumin could be approved as a protective agent that reverses the toxic effect of paracetamol during gestation. Additional research will be conducted to elucidate the specific mechanisms and pathways by which curcumin mitigates paracetamol's effects [41]. Hosseini *et al.* (2025) described the potential of curcumin in mitigating acetaminophen-induced liver damage. The evidence suggests that curcumin could be a promising intervention to mitigate the harmful effects of APAP overdose and improve liver health. However, further research is required to assess the optimal dosing and timing of curcumin administration in APAP toxicity [42]. Hussein *et al.* (2022) evaluated the hepatoprotective effect of curcumin-loaded solid lipid nanoparticles against paracetamol overdose toxicity, focusing on the role of inducible nitric oxide synthase. Cur-loaded SLNs effectively prevented the liver damage induced by PCM overdose through alleviating oxidative stress and inhibiting the serum and hepatic iNOS expression in an effect comparable to NAC and better than raw Cur [43]. Damayanti *et al.* (2023) described the effect of curcumin nanoparticles on paracetamol-induced liver injury in male Wistar rats. Curcumin nanoparticles showed better hepatoprotective ability than pure curcumin [44].

In the current study, we assessed CUR Microsponges' hepatoprotective properties against acute liver damage from PCM overdose, which can cause a range of toxicological changes in adult male albino rats. In the current investigation, adult male albino rats received 2 g/kg of PCM, which increased ALT, AST, and ALP levels. Widely established, elevated levels of the hepatocyte damage marker enzymes AST and ALT are critical indicators of liver injury. Patients with liver disease who had elevated levels of ALP showed pathological changes in biliary flow. The histopathological investigation has verified the elevated ALT levels. Research indicates that curcumin can neutralise reactive oxygen species, inhibit lipid peroxidation, and modify various signalling pathways associated with ALT, AST, and ALP in the paracetamol-treated group compared with the control group, suggesting hepatotoxicity. When we compared CUR microsponges to plain curcumin, our results showed that they protected the liver against PCM-induced damage. CUR microsponges demonstrated this by dramatically lowering levels of AST, ALT, and ALP. PCM may have reduced the number of hepatocytes responsible for protein synthesis, leading to lower serum total protein levels. This may have occurred because of apoptosis and necrosis.

Furthermore, hepatocyte activity was associated with the increase in serum total bilirubin, suggesting that the hepatotoxicant was causing red blood cell disintegration. Histopathologic hepatic architecture confirmed these findings, showing significant hydropic hepatocyte degeneration, dilated portal veins, and swollen portal bile ductules. The data stated above also supported these findings. When compared to simple curcumin, curcumin microsponges were able to counteract the altered hepatic cell shape that was brought about by PCM poisoning. Microsponges exerted a hepatoprotective effect that was much greater than that of simple curcumin at the same dosage. Administering plain curcumin at a dosage of 100 mg/kg showed a slight improvement in the adverse effects that paracetamol would have generated in rats. When compared to curcumin, the microsponges at a dosage similar to 100 mg/kg of curcumin revealed greater healing of liver damage in rats. The higher bioavailability of curcumin may be the source of the

improved hepatoprotective activity of curcumin microsponges.

In conclusion, our work showed that curcumin microsponges significantly reduced acute hepatic damage in rats induced by paracetamol. To understand the underlying mechanisms of curcumin's hepatoprotective properties and improve the composition of microsponges for better drug administration, further investigations are necessary. It is important to do clinical studies to see how curcumin and microsponges-curcumin can help people whose livers have been damaged by paracetamol.

4. Conclusion

This investigation's findings suggest that simple curcumin and microsponges-curcumin are effective in preventing paracetamol-induced liver damage in rats. The remarkable improvement in liver function indicators and histological results revealed the protective advantages. The use of microsponges as a delivery mechanism for curcumin enhances its therapeutic potential by enabling continuous release and targeted delivery to the liver. Based on the current research, we can conclude that curcumin microsponges demonstrated greater hepatoprotective efficacy than regular curcumin in mitigating paracetamol-induced liver damage in experimental rats.

Ethics approval

Ethical Approval Number Provided in Manuscript. The CCSEA's housing regulations were followed. The institution's IAEC approved the study's methodology, (SSDJ/IAEC/2022-23/03).

Acknowledgment

The authors would like to thank the Principal and Secretary of Shreeshakti Shaikshanik Sanstha's Divine College of Pharmacy, Satana, Nashik, India.

Conflict of interest

The author declare that I have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

All required data is available.

Authors Contributions

Equal contribution of all authours.

Authors Orcid numbers:

Gaurav N. Kasar: [0000-0001-6098-2956](https://orcid.org/0000-0001-6098-2956)

Khemchand R. Surana: [0000-0001-8918-1159](https://orcid.org/0000-0001-8918-1159)

Pooja B. Rasal: [0009-0003-3138-7340](https://orcid.org/0009-0003-3138-7340)

Aman B. Upaganlawar: [0000-0003-4122-5081](https://orcid.org/0000-0003-4122-5081)

Manoj S. Mahajan: [0000-0003-4204-2666](https://orcid.org/0000-0003-4204-2666)

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Using artificial intelligence chatbots

There was no use of artificial intelligence in the making of this article.

References

1. Udomsinprasert W, Jittikoon J. Vitamin D and liver fibrosis: Molecular mechanisms and clinical studies. *Biomed. Pharmacother.* (2019); 109: 1351-60.
2. Dinesh K, Sivakumar V, Selvapriya B, Deepika E, Sadiq AM. Evaluation of hepatoprotective polyherbal formulations contains some Indian medicinal plants. *J. Pharmacog. Phytochem.* (2014); 3(4). 1-5.
3. Li J, Fan JG. Characteristics and mechanism of liver injury in 2019 coronavirus disease. *J. Clin. Transl. Hepatol.* (2020); 8(1): 13.
4. Girish C, Koner BC, Jayanthi S, Ramachandra Rao K, Rajesh B, Pradhan SC. Hepatoprotective activity of picroliv, curcumin and ellagic acid compared to silymarin on paracetamol induced liver toxicity in mice. *Fundam. Clin. Pharmacol.* (2009); 23(6): 735-45.
5. Bessems JG, Vermeulen NP. Paracetamol (acetaminophen)-induced toxicity: molecular and biochemical mechanisms, analogues and protective approaches. *Crit. Rev. Toxicol.* (2001); 31:55-138.
6. Sonawane VN, Yeola CA, Sonawane VN, Surana KR, Patil DM, Sonawane DD. Estimation of Paracetamol in various brands of Paracetamol Tablets and their Comparative Study. *Asian J. Pharm. Ana.* 2023; 13:155-61.
7. Kwan D, Bartle WR, Walker SE. Abnormal serum transaminases following therapeutic doses of acetaminophen in the absence of known risk factors. *Dig. Dis. Sci.* (1995); 40:1951-5.
8. Coen M. Metabolic phenotyping applied to pre-clinical and clinical studies of acetaminophen metabolism and hepatotoxicity. *Drug Metab. Rev.* (2015); 47:29-44.
9. Ojo OO, Kabutu FR, Bello M, Babayo U. Inhibition of paracetamol-induced oxidative stress in rats by extracts of lemongrass (*Cymbopogon citratus*) and green tea (*Camellia sinensis*) in rats. *Afr. J. Biotechnol.* (2006); 5: 1227-32.
10. Ahmed S, Rahman A, Alam A, Saleem M, Athar M, Sultana S. Evaluation of the efficacy of *Lawsonia alba* in the alleviation of carbon tetrachloride-induced oxidative stress. *J. Ethnopharmacol.* (2000); 69:157-64.
11. Xu Y, Lin D, Li S, Li G, Shyamala SG, Barish PA, Vernon MM, Pan J, Ogle WO. Curcumin reverses impaired cognition and neuronal plasticity induced by chronic stress. *Neuropharmacol.* (2009); 57:463-71.
12. Yu W, Wu J, Cai F, Xiang J, Zha W, Fan D, Guo S, Ming Z, Liu C. Curcumin alleviates diabetic cardiomyopathy in experimental diabetic rats. *PloS one.* (2012); 7:e52013.
13. Jain A, Samyikutty A, Jackson C, Browning D, Bollag WB, Thangaraju M, Takahashi S, Singh SR. Curcumin inhibits PhIP induced cytotoxicity in breast epithelial cells through multiple molecular targets. *Cancer lett.* (2015); 365:122-31.
14. Surana KR, Patil DM, Sonawane DD, Bachhav PS, Salave MR, Nikam PD. Review on Nanosponges in Cancer Therapy. *MedicoPharmaceutica (MedicoPharm).* (2023); 1:22-31.
15. Luthra PM, Lal N. Prospective of curcumin, a pleiotropic signalling molecule from *Curcuma longa* in the treatment of Glioblastoma. *Eur. J. Med. Chem.* (2016); 109: 23-35.
16. Samini F, Samarghandian S, Borji A, Mohammadi G. Curcumin pretreatment attenuates brain lesion size and improves neurological function following traumatic brain injury in the rat. *Pharmacol. Biochem. Behav.* (2013); 110: 238-44.
17. Fakir JS, Ahire CM, Surana KR, Kalam A, Ahamad AA, Davanage MD. Formulation and Evaluation of Antibacterial and Anti-Inflammatory Emulgel Containing *Eugenia caryophyllus* Buds Extract. *Biosci. Biotechnol. Res. Asia.* (2024); 21:1183-96.
18. Ahire ED, Surana KR, Sonawane VN, Talele SG, Kshirsagar SJ, Laddha UD, Talele GS. Role of Synthetic Medicines as Immunomodulators for the Cure of COVID-19. In *COVID-19 and Immunomodulation with Special Emphasis on Nutraceutical and Herbal Formulation*. Apple Academic Press. 2023; 181-194.
19. Wu GQ, Chai KQ, Zhu XM, Jiang H, Wang X, Xue Q, Zheng AH, Zhou HY, Chen Y, Chen XC, Xiao JY. Anticancer effects of curcumin on lung cancer through the inhibition of EZH2 and NOTCH1. *Oncotarget.* (2016); 7: 26535.
20. Bao W, Li K, Rong S, Yao P, Hao L, Ying C, Zhang X, Nussler A, Liu L. Curcumin alleviates ethanol-induced hepatocytes oxidative damage involving heme oxygenase-1 induction. *J. ethnopharmacol.* (2010); 128: 549-53.
21. Nabavi SF, Daglia M, Moghaddam AH, Habtemariam S, Nabavi SM. Curcumin and liver disease: from chemistry to medicine. *Compr. Rev. Food Sci. Food Saf.* (2014); 13: 62-77.

22. García-Niño WR, Pedraza-Chaverri J. Protective effect of curcumin against heavy metals-induced liver damage. *Food Chem. Toxicol.*(2014); 69:182-201.
23. Naksuriya O, Okonogi S, Schiffelers RM, Hennink WE. Curcumin nanoformulations: a review of pharmaceutical properties and preclinical studies and clinical data related to cancer treatment. *Biomater.*(2014); 35:3365-83.
24. Prasad S, Tyagi AK, Aggarwal BB. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. *Cancer research and treatment: official journal of Korean Cancer Association.* (2014); 46:2-18.
25. Siviero A, Gallo E, Maggini V, Gori L, Mugelli A, Firenzuoli F, Vannacci A. Curcumin, a golden spice with a low bioavailability. *J. Herb. Med.*(2015); 5: 57-70.
26. Osmani RA, Aloorkar NH, Ingale DJ, Kulkarni PK, Hani U, Bhosale RR, Dev DJ. Microsponges based novel drug delivery system for augmented arthritis therapy. *Saudi Pharm. J.*(2015); 23:562-72.
27. Jangde R. Microsponges for colon targeted drug delivery system: An overview. *Asian J. Pharm. Technol.* 2011; 1:87-93.
28. Amrutiya N, Bajaj A, Madan M. Development of microsponges for topical delivery of mupirocin. *AapsPharmscitech.*(2009); 10: 402-9.
29. Jain V, Singh R. Dicyclomine-loaded Eudragit®-based microsphere with potential for colonic delivery: preparation and characterization. *Trop. J. Pharm. Res.*(2010); 9: 67-72.
30. Lahon K, Das S. Hepatoprotective activity of *Ocimum sanctum* alcoholic leaf extract against paracetamol-induced liver damage in Albino rats. *Pharmacog. Res.*(2011); 3:13-8.
31. Sayed MM, El-Kordy EA. The protective effect of curcumin on paracetamol-induced liver damage in adult male rabbits: biochemical and histological studies. *Egypt. J. Histol.*(2014); 37:629-39.
32. Du K, Ramachandran A, Jaeschke H. Oxidative stress during acetaminophen hepatotoxicity: Sources, pathophysiological role and therapeutic potential. *Redox Biol.* 2016; 10:148-56.
33. Farghaly HS, Hussein MA. Protective effect of curcumin against paracetamol-induced liver damage. *Aust. J. Basic Appl. Sci.*(2010);4:4266-74.
34. Maiti K, Mukherjee K, Gantait A, Saha BP, Mukherjee PK. Curcumin-phospholipid complex: preparation, therapeutic evaluation and pharmacokinetic study in rats. *Int.J.Pharm.*(2007); 330:155-63.
35. McGill MR, Jaeschke H. Metabolism and disposition of acetaminophen: recent advances in relation to hepatotoxicity and diagnosis. *Pharm. Res.*(2013); 30:2174-87.
36. Islam R, Alam MJ. Evaluation of liver protective activity of *Moringa oleifera* bark extract in paracetamol induced hepatotoxicity in rats. *BioRxiv.*(2019); 513002.
37. Eldutar E, Kandemir FM, Kucukler S, Caglayan C. Restorative effects of Chrysin pretreatment on oxidant-antioxidant status, inflammatory cytokine production, and apoptotic and autophagic markers in acute paracetamol-induced hepatotoxicity in rats: an experimental and biochemical study. *J. Biochem. Mol. Toxicol.* (2017); 31:e21960.
38. Hamid A, Lee LS, Karim SR, Jufri NF. Hepatoprotective effects of zerumbone against paracetamol-induced acute hepatotoxicity in rats. *Malays. J. Med. Sci.*(2018); 25:64.
39. Yousef MI, Omar SA, El-Guendi MI, Abdelmegid LA. Potential protective effects of quercetin and curcumin on paracetamol-induced histological changes, oxidative stress, impaired liver and kidney functions and haematotoxicity in rat. *Food Chem. Toxicol.*(2010); 48:3246-61.
40. Kannan N, Sakthivel KM, Guruvayoorappan C. Protective Effect of *Acacia nilotica* (L.) against Acetaminophen-Induced Hepatocellular Damage in Wistar Rats. *Adv. Pharmacol. Pharma. Sci.*(2013);2013:987692.
41. Abd El Rahman HA, Ali DM, Omar AR. Evaluation of the potential effect of curcumin and/or paracetamol in pregnant wistar rats and their fetuses. *Egypt. J. Zool.*(2025);83(83):44-58.
42. Einafshar E, Bahrami P, Pashaei F, Naseri P, Ay Gharanjik A, Mirteimoori A, Daraeebaf N, Marami Y, Sahebkar A, Hosseini H. The potential of curcumin in mitigating acetaminophen-induced liver damage. *Naunyn-Schmiedeberg's Arch Pharmacol.* (2025); 1-20.
43. Hussein RM, Kandeil MA, Mohammed NA, Khallaf RA. Evaluation of the hepatoprotective effect of curcumin-loaded solid lipid nanoparticles against paracetamol overdose toxicity: Role of inducible nitric oxide synthase. *J. Liposome Res.*(2022);32(4):365-75.
44. Damayanti IP, Susilaningsih N, Nugroho T, Suhartono S, Suryono S, Susanto H, Suwondo A, Mahati E. The effect of curcumin nanoparticles on paracetamol-induced liver injury in male Wistar rats. *Pharm. Nanotechnol.* 2023;11(5):493-503.