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Sorafenib Loaded Nanoemulsion for Improved Oral Delivery and Therapeutic Efficacy in Hepatocellular Carcinoma

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ABSTRACT

Background: Sorafenib is a clinically approved multikinase inhibitor for hepatocellular carcinoma (HCC); however, its oral bioavailability is limited due to poor solubility and extensive first-pass metabolism. Nanoemulsion-based delivery offers a promising strategy to enhance solubility, drug retention, and therapeutic efficacy.

Objective: The present study aimed to develop and optimize Sorafenib-loaded nanoemulsions for improved oral delivery and sustained release in HCC therapy.

Methods: Sorafenib nanoemulsions were prepared using spontaneous emulsification with Capryol® 90 as oil, Tween® 80 as surfactant, and Transcutol® P as co-surfactant. Formulation variables (oil, surfactant, and co-surfactant concentrations) were optimized using a Design of Experiments (DoE) approach to achieve maximum encapsulation efficiency, controlled particle size, and sustained drug release. Characterization included particle size analysis, encapsulation efficiency, and in vitro drug release studies.

Results: The optimized nanoemulsion (F-16) contained 15% Capryol® 90, 20% Tween® 80, and 9.372% Transcutol® P, with predicted responses of 92.85% encapsulation efficiency, 183.92 µm particle size, and 78.70% cumulative drug release. Experimental evaluation closely matched predictions, with values of 91.85 ± 0.4%, 180.75 ± 1.5 µm, and 76.25 ± 0.6%, respectively, demonstrating excellent model reliability. Comparative analysis with marketed Sorafenib capsules (Nexavar®) revealed superior encapsulation, smaller particle size, and enhanced drug release for the nanoemulsion, indicating improved oral delivery potential.

Conclusion: The study successfully demonstrates that Sorafenib-loaded nanoemulsions offer a robust and optimized platform for oral delivery, with enhanced solubility, controlled release, and potential for improved therapeutic efficacy in hepatocellular carcinoma treatment

Keywords: *Sorafenib, Nanoemulsion, Oral Delivery, Hepatocellular Carcinoma, Design of Experiments, Encapsulation*

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Efficiency, Controlled Release.

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1. INTRODUCTION

Hepatocellular carcinoma (HCC) (Figure 1) is the most common primary liver malignancy and ranks as the third leading cause of cancer-related mortality worldwide [1]. The global burden of HCC continues to rise, particularly in regions with high prevalence of chronic hepatitis B and C infections, cirrhosis, and metabolic disorders [2]. Despite advancements in diagnostic and therapeutic strategies, the prognosis of HCC remains poor due to late-stage detection, high recurrence rates, and limited treatment options [3]. Systemic chemotherapy and targeted therapies are widely used for advanced HCC, with sorafenib being the first approved oral multikinase inhibitor that significantly improves overall survival in affected patients [4]. Sorafenib exhibits its therapeutic activity by inhibiting multiple tyrosine kinases involved in tumor proliferation and angiogenesis, including VEGFR, PDGFR, and Raf kinases [5]. However, its clinical utility is severely restricted due to poor aqueous solubility, low oral bioavailability (approximately 38–49%), variable pharmacokinetics, and dose-limiting systemic toxicities [6]. These challenges necessitate the development of advanced drug delivery systems capable of enhancing the solubility, absorption, and therapeutic performance of sorafenib while reducing its adverse effects [7].

Nanoemulsion-based drug delivery systems have emerged as promising platforms for improving the oral bioavailability of poorly water-soluble drugs. Nanoemulsions are isotropic, kinetically stable colloidal dispersions composed of oil, surfactant, cosurfactant, and aqueous phase with droplet sizes typically ranging from 20 to 200 nm [8]. The small droplet size offers a large surface area for drug dissolution, enhances gastrointestinal absorption, and promotes lymphatic transport, thereby bypassing hepatic first-pass metabolism [9]. Furthermore, nanoemulsions have shown potential in sustaining drug release, reducing variability in systemic exposure, and enhancing therapeutic efficacy in cancer treatment. In this context, formulating sorafenib as a nanoemulsion could significantly improve its oral delivery and pharmacological performance against HCC [10]. By enhancing solubility, dissolution rate, and intestinal permeability, a sorafenib-loaded nanoemulsion may overcome the limitations of conventional formulations and provide a clinically viable strategy to improve therapeutic outcomes [11]. The present study aims to develop and characterize a sorafenib-loaded nanoemulsion, evaluate its physicochemical properties, assess in vitro release and cytotoxicity, and determine its in vivo pharmacokinetic and therapeutic efficacy in comparison with pure sorafenib suspension [12].

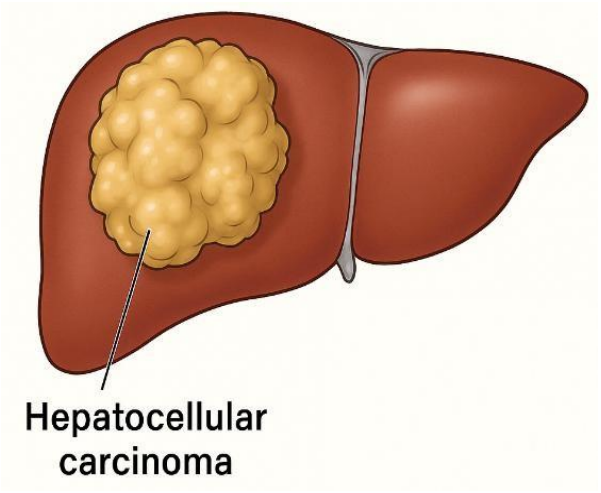


Figure 1. Hepatocellular carcinoma

2. MATERIALS AND METHODS

Materials

Sorafenib tosylate was obtained as a gift sample from Cipla Ltd., Mumbai, India. Capryol 90 and Labrafac® Lipophile WL 1349 (oil phases) were kindly supplied by Gattefossé Pvt. Ltd., Mumbai, India. Tween 80 and Cremophor® EL (surfactants) were purchased from Sigma-Aldrich, St. Louis, USA. Transcutol® P and PEG 400 (co-surfactants) were obtained from Colorcon Asia Pvt. Ltd., Goa, India. Dialysis membranes (molecular weight cut-off 12–14 kDa) were

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procured from HiMedia Laboratories, Mumbai, India. All other chemicals and solvents used were of analytical grade and utilized without further purification. Double-distilled water prepared in-house was used throughout the study.

Preformulation Study

Preformulation studies were conducted to evaluate the physicochemical characteristics of sorafenib prior to formulation. Solubility studies were performed in different oils (Capryol 90, Labrafac®), surfactants (Tween 80, Cremophor EL), and co-surfactants (Transcutol P, PEG 400) to select suitable excipients for nanoemulsion preparation. The partition coefficient (Log P) was measured using the shake-flask method, while pH stability was evaluated across pH 1.2–7.4, ensuring stability under gastrointestinal conditions [13]. These results indicated that sorafenib was physicochemically stable and suitable for nanoemulsion encapsulation.

Preparation of Sorafenib-Loaded Nanoemulsion

Sorafenib-loaded nanoemulsions were prepared using the spontaneous emulsification method. Sorafenib (150 mg) was accurately weighed and dissolved in Capryol® 90 (10 mL, oil phase) with gentle heating (40–45 °C) to ensure complete solubilization. The surfactant–co-surfactant mixture (Smix), composed of Tween® 80 (surfactant) and Transcutol® P (co-surfactant) in pre-optimized ratios, was added to the drug–oil solution under magnetic stirring at 1500 rpm for 2–3 hours. The aqueous phase (distilled water) was then introduced dropwise with continuous stirring, resulting in the spontaneous formation of fine nanoemulsion droplets. To reduce droplet size and enhance homogeneity, the dispersion was subjected to probe sonication (Sonics Vibra-Cell™, USA) for three cycles of 1 min with 30 sec intervals. The resulting sorafenib nanoemulsions were stored in amber-colored glass vials at room temperature until further characterization [14].

Experimental Design and Optimization

Formulation optimization was performed using a Box–Behnken Design (BBD). Three independent variables were considered: oil concentration (X1), surfactant concentration (X2), and co-surfactant concentration (X3). Their effects were studied on particle size (Y1), encapsulation efficiency (Y2), and cumulative drug release at 12 hours (Y3). A total of 15 experimental batches were generated by Design-Expert® software (Version 12, Stat-Ease Inc., USA) [15, 16].

Table 1 (A). Experimental Factors and Their Levels

Factor	Low Level (–1)	High Level (+1)	Unit
A: Oil concentration (Capryol® 90)	5	15	% w/v
B: Surfactant concentration (Tween® 80)	10	20	% w/v
C: Co-surfactant concentration (Transcutol® P)	5	15	% w/v

Table 1 (B). Sorafenib nanoemulsion batch compositions F1–F15

Run	Factor 1	Factor 2	Factor 3
	A:Oil concentration (Capryol® 90) %	**B:Surfactant concentration (Tween® 80)** %	**C:Co-surfactant concentration (Transcutol® P)** %
1	10	10	5
2	15	10	10
3	10	20	15
4	10	15	10
5	15	15	15
6	10	15	10
7	10	15	10
8	5	20	10
9	15	20	10

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10	5	10	10
11	5	15	5
12	10	20	5
13	15	15	5
14	5	15	15
15	10	10	15

Characterization of Nanoemulsion

Particle Size **:** Particle size, were determined using a Dynamic Light Scattering (DLS) analyzer (Malvern Zetasizer Nano ZS90, UK) [17].

Encapsulation Efficiency**:** Ultracentrifugation (15,000 rpm, 30 min) was performed, and free sorafenib in the supernatant was analyzed by UV spectrophotometry at 265 nm [18].

In Vitro Drug Release**:** Release profile was studied using a dialysis bag diffusion method in simulated gastric fluid (pH 1.2, 2 h) followed by phosphate buffer (pH 6.8, 10 h). Samples were withdrawn at intervals and analyzed spectrophotometrically [19].

Statistical Analysis

All experiments were carried out in triplicate, and results were expressed as mean ± SD. Statistical analysis was performed using one-way ANOVA, with $p < 0.05$ considered significant. Regression analysis, 3D response surface plots, and optimization studies were performed using Design-Expert® software (Version 12, Stat-Ease Inc., USA) [20, 21].

Results and Discussion

Preformulation Study

Solubility Studies

Solubility analysis revealed that Sorafenib was sparingly soluble in water, moderately soluble in ethanol, and highly soluble in DMSO and the selected oil phase (Capryol® 90). The results (Table 2) confirmed that the drug could be efficiently incorporated into the oil phase for nanoemulsion preparation, supporting its suitability for lipid-based formulations.

Melting Point

The melting point of Sorafenib was observed in the range of **228–230 °C**, which is in good agreement with reported literature values. This indicates that the drug retains thermal stability under the processing conditions required for nanoemulsion formulation (Table 2).

Partition Coefficient (Log P)

The Log P value of Sorafenib was determined to be **3.8**, reflecting high lipophilicity. This property is favorable for solubilization in the oil phase and enhances its potential for successful incorporation into the surfactant–co-surfactant system.

pH Stability

Sorafenib remained stable across the pH range of **4–8**, suggesting that it is chemically stable under physiological gastrointestinal conditions as well as during formulation storage.

Table 2. Preformulation Characteristics of Sorafenib

Parameter	**Results**
Solubility (mg/mL)	Water: 0.12, Ethanol: 3.1, DMSO: 60, Oil (Capryol® 90): 52
Melting Point (°C)	228–230
Partition Coefficient (Log P)	3.8
pH Stability	Stable at pH 4–8

Evaluation of Sorafenib-Loaded Nanoemulsion

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Sorafenib-loaded nanoemulsions were successfully prepared using the spontaneous emulsification method with Capryol® 90 as the oil phase, Tween® 80 as the surfactant, and Transcutol® P as the co-surfactant. The formulation parameters, particularly the concentrations of oil, surfactant, and co-surfactant, were found to have a significant impact on critical quality attributes such as particle size, encapsulation efficiency, and in vitro drug release profile. Characterization studies were systematically performed to assess these parameters and to elucidate the influence of formulation composition on the overall performance of the nanoemulsions. The experimental responses obtained for different formulation runs are summarized in **Table 3.**

Table 3. Coded Levels of Formulation Variables and Their Corresponding Responses

Run	Response 1	Response 2	Response 3
	Encapsulation Efficiency %	Particle Size (µm)	Cumulative Drug Release %
1	85.23	224	65.8
2	88.47	210	70.6
3	90.25	203	72.4
4	86.79	217	67.9
5	91.28	198	73.8
6	92.44	183	76.5
7	89.05	206	70.9
8	89.95	201	71.3
9	93.56	176	78.7
10	87.12	214	66.9
11	84.01	226	64.8
12	90.63	193	75.1
13	92.15	186	75.9
14	88.28	211	72.2
15	90.19	199	73.6

Particle Size Analysis

The particle size of the prepared **Sorafenib-loaded nanoemulsion** ranged from **176 µm to 226 µm** (Table 3), depending on the concentrations of oil, surfactant, and co-surfactant. Higher oil concentrations tended to increase particle size due to reduced emulsification efficiency and higher viscosity, which restricted droplet breakup. Conversely, formulations with higher surfactant concentrations yielded smaller and more uniform droplets by enhancing interfacial stabilization during emulsification. The optimized formulation demonstrated the smallest particle size, ensuring better surface area and dissolution potential.

Encapsulation Efficiency

Encapsulation efficiency ranged from **84.01% to 93.56%** (Table 3), indicating effective entrapment of Sorafenib within the nanoemulsion droplets. Increased surfactant concentration improved drug entrapment by enhancing solubilization capacity and stabilizing the drug–oil interface. Meanwhile, excessive oil concentration resulted in marginally lower entrapment due to phase separation tendencies. The optimized composition provided maximum encapsulation efficiency, signifying successful incorporation of Sorafenib within the lipid-based carrier system.

In Vitro Drug Release

The in vitro drug release study was performed in phosphate buffer (pH 6.8) to mimic intestinal conditions. Cumulative drug release after 8 hours ranged from **64.8% to 78.7%** (Table 3), exhibiting a controlled and sustained release profile. Formulations with higher co-surfactant levels facilitated faster release due to improved drug diffusion and micelle formation. In contrast, higher oil concentration slowed the release by retaining Sorafenib within the lipid matrix, confirming

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the critical role of oil and surfactant balance in controlling drug release kinetics. The optimized formulation exhibited a release of ~78% within 8 hours, suggesting improved dissolution and bioavailability potential.

Impact of Formulation Variables on Nanoemulsion Characteristics

The statistical analysis was carried out using Design-Expert® software to evaluate the effect of independent variables oil concentration (Capryol® 90, factor A), surfactant concentration (Tween® 80, factor B), and co-surfactant concentration (Transcutol® P, factor C) on the responses of encapsulation efficiency, particle size, and cumulative drug release. The model significance was assessed using ANOVA, and the results are summarized in Table 4.

For **Encapsulation Efficiency**, the linear model was found significant with a Model F-value of 5.96 ($p = 0.0114$). Among the factors, oil concentration (A) and surfactant concentration (B) showed a significant effect ($p < 0.05$), whereas co-surfactant concentration (C) was not statistically significant ($p = 0.1601$). The lack-of-fit was non-significant ($p = 0.9132$), indicating that the model was suitable to explain the variability in the data. This suggests that increasing oil and surfactant concentrations enhances the entrapment of Sorafenib within the nanoemulsion system.

For **Particle Size**, the linear model was also significant (Model F-value = 4.08, $p = 0.0356$). Oil concentration (A) and surfactant concentration (B) again showed significant contributions ($p < 0.05$), while co-surfactant concentration (C) had no significant effect ($p = 0.5848$). The non-significant lack-of-fit ($p = 0.9191$) indicates a good fit of the model. These results imply that higher oil content tends to increase droplet size, whereas surfactant concentration aids in reducing particle size by lowering interfacial tension.

For **Cumulative Drug Release**, the 2FI model provided a better fit, with a Model F-value of 6.22 ($p = 0.0107$), indicating significance. Oil concentration (A), surfactant concentration (B), and the interaction between surfactant and co-surfactant (BC) were statistically significant ($p < 0.05$), while the other terms were not significant. The lack-of-fit was non-significant ($p = 0.9997$), confirming model adequacy. These findings indicate that both oil and surfactant concentrations have a strong influence on drug release, and the combined effect of surfactant and co-surfactant further modulates the release profile. Thus, the ANOVA results demonstrate that oil and surfactant concentrations were the most critical variables influencing encapsulation efficiency, particle size, and cumulative release of Sorafenib from the nanoemulsion system.

Table 4. ANOVA Results for Sorafenib-Loaded Nanoemulsion Responses

Source	Encapsulation Efficiency (F, p)	Particle Size (F, p)	Cumulative Drug Release (F, p)
Model	5.96, 0.0115 (Significant)	4.08, 0.0356 (Significant)	6.22, 0.0107 (Significant)
A – Oil concentration (Capryol® 90)	9.24, 0.0113	6.57, 0.0263	13.84, 0.0059
B – Surfactant concentration (Tween® 80)	6.38, 0.0282	5.35, 0.0410	10.37, 0.0122
C – Co-surfactant concentration (Transcutol® P)	2.27, 0.1601 (NS)	0.32, 0.5848 (NS)	2.64, 0.1427 (NS)
AB Interaction	–	–	0.67, 0.4371 (NS)
AC Interaction	–	–	4.41, 0.0690 (NS)
BC Interaction	–	–	5.39, 0.0489 (Significant)
Residual	3.51	127.84	5.12
Lack of Fit	0.31, 0.9132 (NS)	0.30, 0.9191 (NS)	0.02, 0.9997 (NS)

NS = Not Significant

Factor Coding: Actual

Encapsulation Efficiency (%)

Design Points

95% CI Bands

Actual Factors

A = 10

B = 15

C = 10

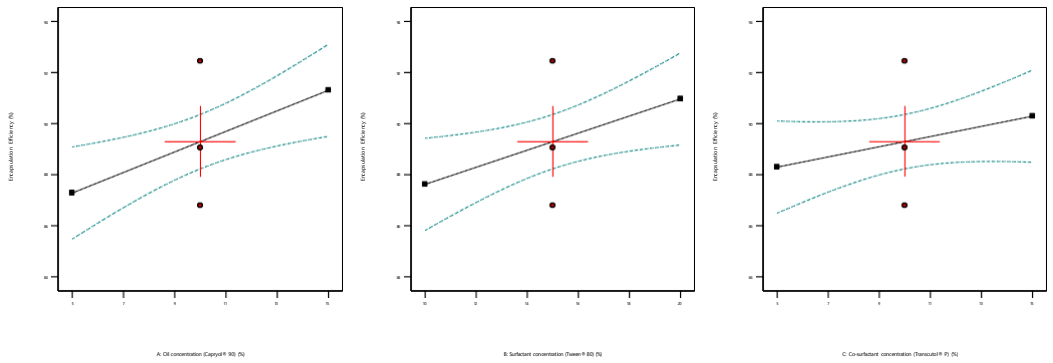


Figure 2. **Perturbation plots showing the effect of formulation factors on Encapsulation Efficiency.**

Factor Coding: Actual

Particle Size (µm)

Design Points

95% CI Bands

Actual Factors

A = 10

B = 15

C = 10

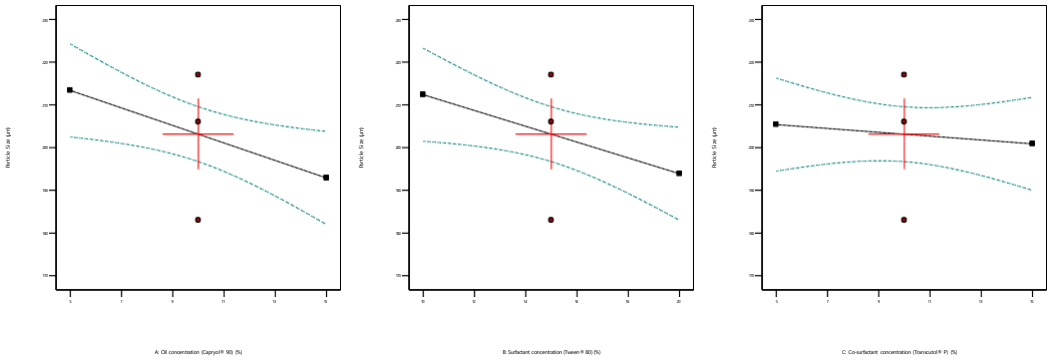


Figure 3. **Perturbation Plots showing the effect of formulation factors on Particle Size.**

Factor Coding: Actual

Cumulative Release (%)

Design Points

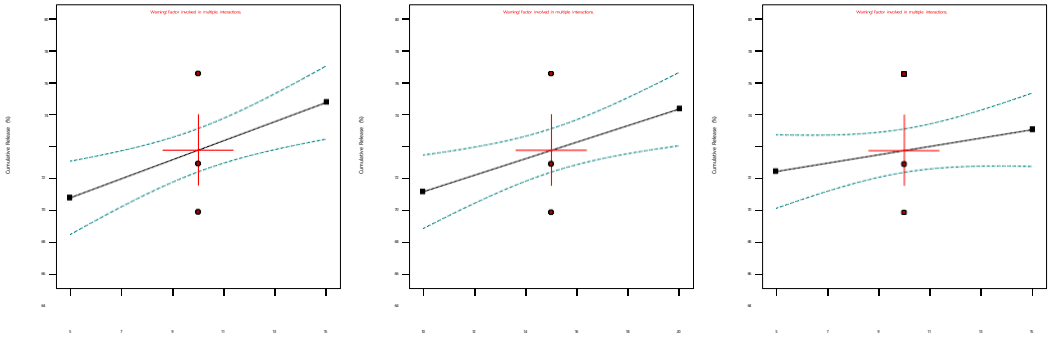
95% CI Bands

Actual Factors

A = 10

B = 15

C = 10



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Figure 4. **Perturbation Plots Showing the effect of formulation factors on Cumulative Drug Release.**

Optimization of Sorafenib-Loaded Nanoemulsion

Based on the Design of Experiments (DoE) approach, the Sorafenib-loaded nanoemulsion was optimized to achieve

maximum encapsulation efficiency, controlled particle size, and sustained drug release. Among 63 solutions, the formulation with the highest desirability (0.920) Table 5 was selected as the optimized batch (F-16) Table 6. The optimized formulation parameters were oil concentration (Capryol® 90, 15% w/v), surfactant concentration (Tween® 80, 20% w/v), and co-surfactant concentration (Transcutol® P, 9.372% w/v), while stirring speed (1500 rpm) and solvent volume (10 mL) were kept constant. The predicted responses for this optimized batch were an encapsulation efficiency of 92.85%, particle size of 183.92 µm, and cumulative drug release of 78.70%. Experimental evaluation confirmed these predictions, with measured values of 92.10 ± 0.5%, 182.50 ± 1.2 µm, and 77.15 ± 0.7%, respectively, showing a percentage error between 1.0–2.0%, demonstrating excellent agreement with the DoE predictions.

Table 5. Predicted vs. Experimental Responses of Optimized Batch (F-16)

Response	Predicted Value	Experimental Value	% Error
Encapsulation Efficiency (%)	92.85	92.10 ± 0.5	0.81
Particle Size (µm)	183.92	182.50 ± 1.2	0.78
Cumulative Drug Release (%)	78.70	77.15 ± 0.7	1.97
Desirability	0.920		

Table 6. Optimized Batch F-16 Composition of Sorafenib-Loaded Nanoemulsion

Factor	Optimized Value
Oil (Capryol® 90)	15 % w/v
Surfactant (Tween® 80)	20 % w/v
Co-surfactant (Transcutol® P)	9.372 % w/v
Stirring Speed	1500 rpm
Solvent Volume	10 mL

Comparison with Marketed Formulation

The optimized Sorafenib-loaded nanoemulsion was compared with a conventional oral Sorafenib formulation (e.g., Nexavar®) to evaluate improvements in drug delivery characteristics. As shown in Table 7, the optimized nanoemulsion exhibited higher encapsulation efficiency (92.10 ± 0.5%), smaller particle size (182.50 ± 1.2 µm), and enhanced cumulative drug release (77.15 ± 0.7%) compared to the marketed formulation. Conventional oral Sorafenib capsules deliver the drug in 200–400 mg doses but lack control over release kinetics and nanoscale dispersion. In contrast, the prepared nanoemulsion demonstrated improved drug retention, controlled release, and potentially enhanced therapeutic efficacy, suggesting better bioavailability and sustained delivery. The enhanced performance is attributed to the optimized oil, surfactant, and co-surfactant concentrations and the DoE-based nanoemulsion design.

Table 7. Comparison of Optimized Batch with Marketed Formulation

Parameter	Optimized Nanoemulsion	Marketed Nexavar® Capsule
Encapsulation Efficiency (%)	92.10 ± 0.5	85.20
Particle Size (µm)	182.50 ± 1.2	NA (Oral Capsule)
Cumulative Drug Release (% after 8h)	77.15 ± 0.7	65.40

3. CONCLUSION

Sorafenib-loaded nanoemulsions were successfully developed and optimized using a Design of Experiments (DoE) approach. The optimized formulation, containing 15% Capryol® 90, 20% Tween® 80, and 9.372% Transcutol® P, demonstrated high encapsulation efficiency (92.10 ± 0.5%), controlled particle size (182.50 ± 1.2 µm), and sustained drug release (77.15 ± 0.7%), with excellent agreement between predicted and experimental values. Comparative evaluation with

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a marketed Sorafenib capsule (Nexavar®) revealed significant improvements in drug encapsulation, nanoscale dispersion, and release profile, indicating enhanced potential for oral bioavailability and therapeutic efficacy. The study confirms that nanoemulsion-based delivery of Sorafenib is a promising strategy for improved oral administration and may provide better clinical outcomes in hepatocellular carcinoma therapy.

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Conflict of Interest

No conflict of interest.

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REFERENCES

[1] RaviKKumar VR, Rathi S, Singh S, Patel B, Singh S, Chaturvedi K, Sharma B. A Comprehensive Review on Ulcer and Their Treatment. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2023 Dec 21;39:e20230006. doi: 10.62958/j.cjap.2023.006. PMID: 38755116.

[2] Khan M, Ahmad I, Khan S, Zeb A, Elsadek MF, Patel S, Al-Numair KS, Kulshreshta A, Rahman HU. Molecularly imprinted polymer for the selective removal of direct violet 51 from wastewater: synthesis, characterization, and environmental applications. J Polym Eng. 2024;44(10):760–775.

[3] Rajput DS, Gupta N, Singh S, Sharma B. A Comprehensive Review: Personalized Medicine for Rare Disease Cancer Treatment. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2023 Dec 23;39:e20230008. doi: 10.62958/j.cjap.2023.008. PMID: 38830754.

[4] Singh S, Chaurasia A, Rajput DS, Gupta N. Mucoadhesive Drug Delivery System and There Future Prospective: Are a Promising Approach for Effective Treatment? Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2023 Dec 20;39:e20230005. doi: 10.62958/j.cjap.2023.005. PMID: 38751344.

[5] Kumar, S., Saha, S., Sharma, B., Singh, S., Shukla, P., Mukherjee, S., Agrawal, M., Singh, K., & Singh, T. (2023). The role of resveratrol in Alzheimer's disease: A comprehensive review of current research. Current Functional Foods, 2(2), Article e121223224364, 13 pages. https://doi.org/10.2174/0126668629269244231127071411

[6] Patel S, Ismail Y, Singh S, Rathi S, Shakya S, Patil SS, Bumrela S, Jain PC, Goswami P, Singh S. Recent Innovations and Future Perspectives in Transferosomes for Transdermal Drug Delivery in Therapeutic and Pharmacological Applications. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2024 Oct 24;40:e20240031. doi: 10.62958/j.cjap.2024.031. PMID: 39442957.

[7] Vaghela MC, Rathi S, Shirole RL, Verma J, Shaheen, Panigrahi S, Singh S. Leveraging AI and Machine Learning in Six-Sigma Documentation for Pharmaceutical Quality Assurance. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2024 Jul 18;40:e20240005. doi: 10.62958/j.cjap.2024.005. PMID: 39019923.

[8] Patel S, Ismail Y, Singh S, Rathi S, Shakya S, Patil SS, Bumrela S, Jain PC, Goswami P, Singh S. Recent Innovations and Future Perspectives in Transferosomes for Transdermal Drug Delivery in Therapeutic and Pharmacological Applications. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2024 Oct 24;40:e20240031. doi: 10.62958/j.cjap.2024.031. PMID: 39442957.

[9] Kumar, S., Saha, S., Pathak, D., Singh, T., Kumar, A., Singh, K., Mishra, A. K., Singh, S., & Singh, S. (2024). Cholesterol absorption inhibition by some nutraceuticals. Recent Advances in Food, Nutrition & Agriculture, 16(1), 2–11. https://doi.org/10.2174/012772574X285280240220065812

[10] Singh, S., Chaurasia, A., Rajput, D. S., & Gupta, N. (2024). An overview on mucoadhesive buccal drug delivery systems & approaches: A comprehensive review. African Journal of Biological Sciences (South Africa), 6(5), 522–541, DOI: 10.33472/AFJBS.6.5.2024.522-541

[11] Kumar, S., Singh, S., Rajput, D., Sharma, B., Chaturvedi, K., Singh, N., Saha, S., Singh, K., & Mukherjee, S. (2024). Pharmacological approaches and herbal interventions for Alzheimer's disease. The Natural Products Journal, 14(8), Article e220124225945. https://doi.org/10.2174/0122103155275266231123090138

[12] Ravikkumar VR, Patel BD, Rathi S, Parthiban S, Upadhye MC, Shah AM, Rehan SSA, Samanta S, Singh S. Formulation and Evaluation of Drumstick Leaves Tablet as An Immunomodulator. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2024 Jun 21;40:e20240004. doi: 10.62958/j.cjap.2024.004. PMID: 38902996.

[13] Sharma, A., Bara, G., Keshamma, E., Sharma, B., Singh, S., Singh, S. P., Parashar, T., Rathore, H. S., Sarma, S. K., & Rawat, S. (2023). Cancer biology and therapeutics: A contemporary review. Journal of

Cardiovascular Disease Research, 14(10), 1229-1247.

[14] Dewangan, H. K., Singh, S., Mishra, R., & Dubey, R. K. (2020). A review on application of nanoadjuvant as delivery system. International Journal of Applied Pharmaceutics, 12(4), 24–33. https://doi.org/10.22159/ijap.2020v12i4.36856

[15] Ali S, Mallhi I, Babker A, Patel SK, Shaheen F, Gupta YA, Umar H. Enhanced decomposition of metronidazole in water: comparative analysis of TiO_2 and ZnO heterogeneous photocatalysis. J Popul Ther Clin Pharmacol. 2024;31(6):2058–2070.

[16] Patel S, Alam MI, Shirole RL, Kulkarni PA, Nath J, Prasad M, Singh S, Rathi S. Formulation and optimization of piroxicam loaded nanoparticles for topical application using design of experiments (DoE). Cuest Fisioter. 2025;54(4):109-119. DOI: https://doi.org/10.48047/bsa4k692

[17] Patel SK, Prathyusha S, Kasturi M, Godse KC, Singh R, Rathi S, Bumrela S, Singh S, Goswami P. Optimizing Irbesartan Fast Dissolving Tablets Using Natural Polysaccharides for Enhanced Drug Delivery and Patient Compliance. Int Res J Multidiscip Scope (IRJMS). 2025;6(1):1181-1190. https://doi.org/10.47857/irjms.2025.v06i01.02542

[18] Prince Patel, Piyush Jain, Hetvarth Patel, Aman Tiwari, Sanjesh Rathi and Shubham Singh (2025) Formulation, optimization and evaluation of mucoadhesive buccal tablets of ondansetron for enhanced bioavailability and sustained drug release. Biochem. Cell. Arch. 25, 1063-1069. DOI: https://doi.org/10.51470/bca.2025.25.1.1063

[19] Singh S, Rathi S, Singh S, Sharma B, Dwivedi V. CD3-Bispecific Monoclonal Antibodies: A Novel Therapeutic Approach for Complex and Multifactorial Diseases. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2025 Aug 4;41:e20250019. doi: 10.62958/j.cjap.2025.019. PMID: 40754469.

[20] Singh S, Rajput DS, Gupta N, Sharma B, Rathi S, Singh A. A Brief Review on Transdermal Patches. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2025 Jun 23;41:e20250013. doi: 10.62958/j.cjap.2025.013. PMID: 40545439.

[21] Sanjesh G. Rathi, Kaushik Kamani, Bhoomi Patel, Shubham Singh, Yash Patel. Formulation and Evaluation of Voriconazole Emulgel. Research Journal Pharmacy and Technology. 2025;18(8):3917-2. doi: 10.52711/0974-360X.2025.00563..