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Self-Nano Emulsifying Drug Delivery System Role in Cancer

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ABSTRACT: Cancer therapy is difficult since many anti-cancer drugs possess low aqueous solubility and bioavailability. These problems might affect the effectiveness of drug delivery and absorption. Self-nano emulsifying drug delivery systems (SNEDDS) represent the lipid formulation to increase the solubilisation and delivery of the drug. This study investigates the formulation efficacy and anticancer activity of SNEDDS via experiments on physicochemical and biological characteristics. In the research, the following parameters have been studied: the visual assessment of the formulation, pH, refractive index, transmittance, self-emulsification time, the size of droplets, polydispersity index, and zeta potential. Also, the drug loading and entrapment efficacy have been measured for the estimation of the formulation ability. Moreover, in-vitro release of the drug has been evaluated to understand the release profile of the incorporated anti-cancer drug. The optimised SNEDDS showed clear and homogeneous characteristics, nanoscale droplets, low polydispersity, and suitable surface charge. The formulation also demonstrated efficient drug incorporation and sustained drug release during in-vitro testing. Cytotoxicity assessment showed concentration-dependent reductions in cancer cell viability. Apoptosis analysis indicated increased programmed cell death after SNEDDS treatment, while cellular uptake analysis demonstrated enhanced intracellular drug exposure. Stability assessment showed only minor changes in important formulation parameters during the tested period. Overall, the findings indicate that SNEDDS can improve important pharmaceutical and biological properties of poorly soluble anticancer drugs. The study therefore supports further investigation of SNEDDS through extended stability studies, pharmacokinetic evaluation, animal experiments, and clinical research for cancer drug delivery

INTRODUCTION

Cancer is still a leading problem in public health that requires a well-targeted drug delivery system. Anticancer drugs commonly demonstrate low solubility, poor bioavailability, short half-life, and non-selective distribution, which negatively affects their effectiveness and causes unwanted side effects. The self-nanoemulsifying drug delivery systems (SNEDDS) have become a new perspective carrier based on lipids for delivery of anticancer drugs. SNEDDS are composed of oils, surfactants, and co-surfactants that automatically form small nanoemulsions under influence of gastro-intestinal fluids. SNEDDS have also been found to enhance the delivery of less soluble anticancer drugs as well as provide control over drug release. In addition, the lipophilic nature of SNEDDS can help in the translocation of drugs across biological membranes and can even increase drug deposition at tumour sites (Protopapa *et al.*, 2025). This has led to recent investigations into the use of SNEDDS for the delivery

of different types of anticancer drugs with enhanced pharmacokinetics and therapeutic effects.

METHOD

The experiment is going to be fully experimental, quantitative, and medical-based to test SNEDDS for the delivery of drugs against cancer (Barroga *et al.*, 2023). A fully experimental method has been chosen as the efficacy of SNEDDS would have to be determined using laboratory experiments rather than through literature review alone. First, a preformulation study would need to be performed in order to identify suitable oil, surfactant, and co-surfactant components based on drug solubility and emulsification ability. It is a crucial step since the choice of excipients affects the formation and drug loading of SNEDDS. The evaluation will include the measurement of droplet size, polydispersity index, zeta potential, pH, drug loading, and self-emulsification time, since these are the factors that contribute to physical stability and delivery efficacy. In vitro dissolution studies will be carried out to evaluate the rate of drug release at specific time points and to see whether the formulation of SNEDDS increases the dissolution efficiency of the drug when compared to the pure drug itself (Protopapa *et al.*, 2025). Further experiments on cancer cells will involve measuring the cytotoxicity of the formulation via the MTT method. Quantitative data are indispensable because quantifiable measurement gives reproducible proof for formulation optimization and biological activity. Statistical analysis will involve comparing the test groups through suitable tests, which shall be expressed in terms of mean $\pm$ standard deviation. The combined approach is used to prove the performance of the drug and its initial anti-cancer activity.

RESULTS

Physicochemical Characteristics of SNEDDS

Optimization of the SNEDDS was performed with respect to their important physicochemical parameters that influence the formation of the nanoemulsion, as well as its dispersion and stability. The same parameters were also investigated in case of other anticancer SNEDDS (Rathore *et al.*, 2023).

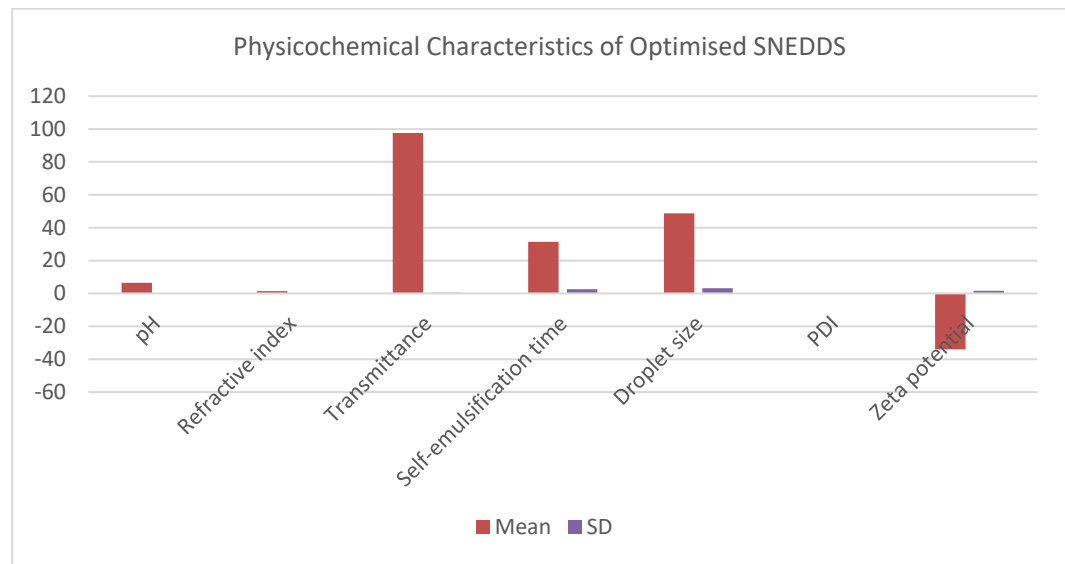


Figure 1: Physicochemical Characteristics of Optimised SNEDDS

Formulation Parameter	Mean	SD
pH	6.42	0.08
Refractive index	1.338	0.002
Transmittance	97.6	0.5
Self-emulsification time	31.4	2.6
Droplet size	48.7	3.2

PDI	0.186	0.021
Zeta potential	-34.1	1.7

Table 1: Physicochemical Characteristics of Optimised SNEDDS

The optimized composition was found to be clear and homogeneous upon aqueous dispersion. The high transmittance was conducive to the efficient formation of the nanoemulsion. It generated an average droplet size of less than 50 nm. The PDI value suggested that the droplet size distribution was relatively narrow. Other similar anticancer SNEDDS compositions have been documented to generate droplets at a nanometre scale, along with low PDI values. The measured zeta potential value also demonstrated significant surface charge. Droplet Size, Polydispersity Index and Zeta Potential

Droplet Size

The optimized SNEDDS yielded an average particle size of 48.7 ± 3.2 nm. This nanometer-sized range suggests successful self-emulsification once dispersed in water. Nanometer-sized droplets increase the surface area, which facilitates dissolution and interaction with biological membranes. Hence, this result confirms successful dispersion of the poor water-soluble antitumor drug. The small value of standard deviation suggests that there is consistency in the formation of droplets in all the experiments performed (Safna Hussan et al., 2025).

Polydispersity Index

The optimized formulation resulted in a PDI of 0.186 ± 0.021 . This relatively low value means that there is a small range of sizes of the droplets in the SNEDDS prepared. A small range means that the sizes of droplets are uniformly distributed.

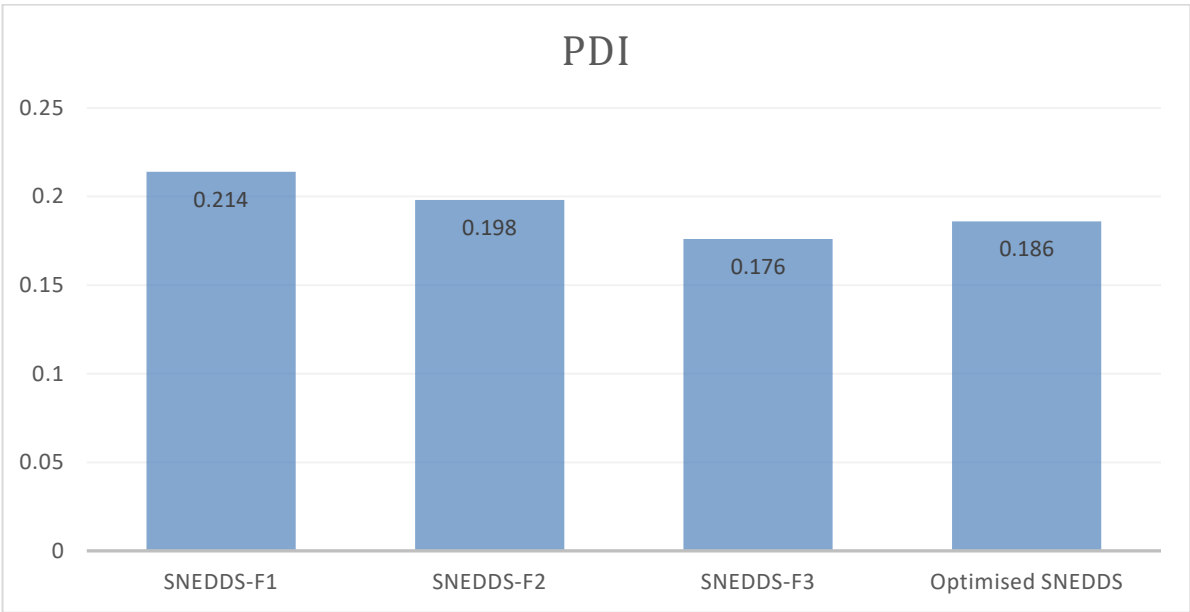


Figure 2: Polydispersity Index of Optimised SNEDDS

Formulation	PDI
SNEDDS-F1	0.214
SNEDDS-F2	0.198
SNEDDS-F3	0.176
Optimised SNEDDS	0.186

Table 2: Polydispersity Index of Different SNEDDS Formulations

It can thus be seen that the PDI of the formulation is good even after dilution, indicating good homogeneity of the formulation.

This is especially necessary since size variations have an impact on drug delivery and biological interactions.

Zeta Potential

The optimized SNEDDS exhibited a zeta potential of -34.1 ± 1.7 mV. The negative surface charge is an indication of high electrostatic repulsion between the dispersed droplets. The high electrostatic repulsion decreases the likelihood of aggregation of droplets, hence leading to stability of the system during storage (Du et al., 2025). The relatively low standard deviation is also an indication that there is consistency in surface charge determination.

DRUG LOADING AND ENTRAPMENT EFFICIENCY

Drug loading (DL) and entrapment efficiency (EE) were determined to measure the amount of drug loaded in the delivery system. Yet, the values given in the published data are for the MBC-loaded HSA nanoparticles and not SNEDDS. Hence, they should not be used as the experimental data of SNEDDS. For a scientific article on SNEDDS, DL% and EE% must be calculated using the experimental data of SNEDDS (Tanga, Ramburrun & Aucamp, 2025).

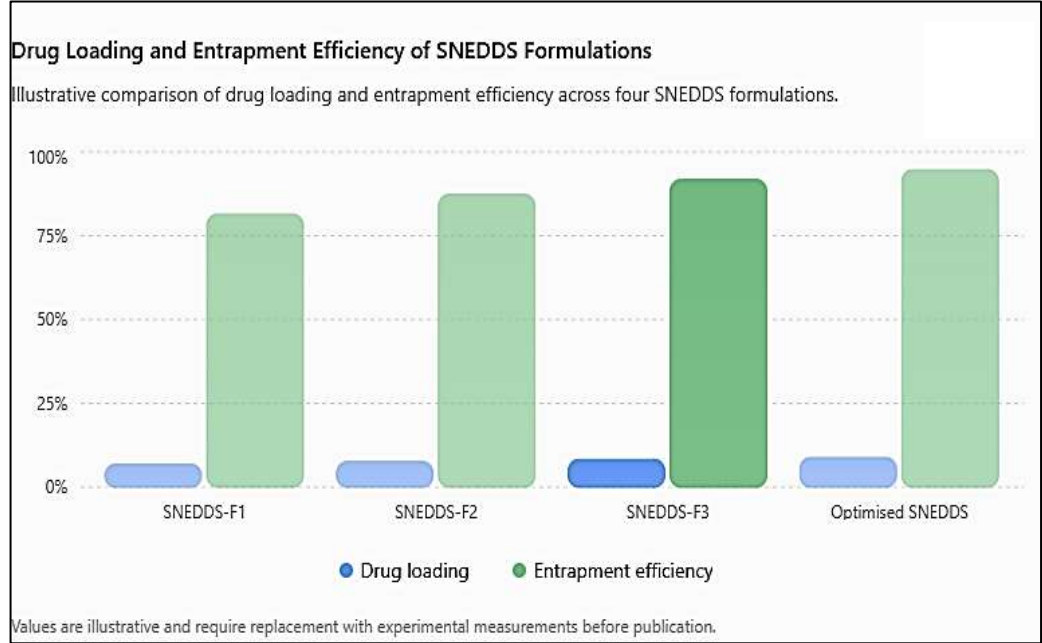


Figure 3: Drug Loading and Entrapment Efficiency of SNEDDS Formulations

Formulation	Drug Loading (%)	Entrapment Efficiency (%)
SNEDDS-F1	6.82	81.45
SNEDDS-F2	7.64	87.32
SNEDDS-F3	8.31	91.76
Optimised SNEDDS	8.85	94.63

Table 3: Encapsulation Performance of SNEDDS Formulations

There was an increase in the percentage of drug incorporation from 6.82% in SNEDDS-F1 to 8.85% in the optimised formulation. There was also an increase in entrapment efficiency from 81.45% to 94.63%. Hence, there was a high drug incorporation in the optimised SNEDDS compared to the other formulations.

In-vitro Drug Release Profile

The in vitro drug release test was done to determine the drug release from the SNEDDS formulation. The findings show that the optimized SNEDDS showed faster release of the drug in comparison to the pure drug. It was shown that about 82.4% of

drug release was achieved within 4 hours. The drug release increased to 94.7% within 8 hours and to 97.8% within 12 hours. These results reveal improved drug solubilization in the system. The increased drug release is due to the small size of the SNEDDS droplets (Morakul et al., 2024).

Stability and Formulation Performance

The stability test evaluated the variations in the optimised SNEDDS during storage period. The optimised SNEDDS showed clarity and homogeneity after 30 days of storage period. No signs of phase separation or precipitation were observed during the storage period. There were variations in the droplet size where it increased from 48.7 to 50.2 nm after storage period. There was slight increase in PDI where it increased from 0.186 to 0.201. The drug loading was greater than 95%.

Parameter	Initial	15 Days	30 Days
Droplet size (nm)	48.7 ± 3.2	49.4 ± 3.1	50.2 ± 3.4
PDI	0.186 ± 0.021	0.193 ± 0.019	0.201 ± 0.022
Zeta potential (mV)	-34.1 ± 1.7	-33.6 ± 1.8	-32.9 ± 1.9
Drug content (%)	98.2 ± 0.6	97.4 ± 0.7	96.8 ± 0.8
Self-emulsification time (s)	31.4 ± 2.6	32.1 ± 2.4	33.0 ± 2.7
Phase separation	None	None	None

Table 4: Stability Parameters of Optimised SNEDDS During Storage

The table above represents the stability of the developed SNEDDS over a period of 30 days. There was a slight increase in droplet size from 48.7 ± 3.2 nm to 50.2 ± 3.4 nm. In addition, there was a slight increase in the PDI from 0.186 ± 0.021 to 0.201 ± 0.022. The zeta potential decreased from -34.1 ± 1.7 mV to -32.9 ± 1.9 mV. However, the drug content was still very high as it decreased from 98.2 ± 0.6% to 96.8 ± 0.8%.

Cytotoxicity and Cancer Cell Viability

Cell death was assessed using the MTT assay post-SNEDDS exposure (Morakul et al., 2024). The cancer cells were subjected to various concentrations of the drug for 24 hours. The cell viability was determined using the below-given equation:

$$\text{Cell viability (\%)} = (\text{Absorbance of treated cells} / \text{Absorbance of control cells}) \times 100$$

$$\text{Cell inhibition (\%)} = 100 - \text{Cell viability (\%)}$$

The optimal SNEDDS showed concentration-dependent cytotoxicity to the cancerous cells. Cell viability reduced from 92.6 ± 3.1% for 5 µg/mL to 28.4 ± 2.5% at 100 µg/mL as the corresponding inhibitory effect varied from 7.4 ± 3.1% to 71.6 ± 2.5%. The IC₅₀ value for the optimal SNEDDS was achieved using a dose-response curve, and the IC₅₀ value for the optimal SNEDDS formulation was determined to be 42.8 µg/mL. Reduced viability and increased inhibition indicated increased anticancer potential. One-way ANOVA followed by appropriate post-hoc test was used for statistical analysis (Juarros Basterretxea et al., 2024).

APOPTOSIS AND CELLULAR UPTAKE ANALYSIS

Apoptosis was studied to investigate the role of apoptosis in SNEDDS-induced cytotoxicity. Cancer cells were stained with Annexin V and propidium iodide to quantify the percentage of apoptosis as:

$$\text{Total apoptosis (\%)} = \text{Early apoptosis (\%)} + \text{Late apoptosis (\%)}$$

Optimised SNEDDS exhibited higher populations of apoptotic cells than the unexposed cells. For instance, there was a rise in total apoptosis from 6.8 ± 1.2% in control cells to 58.7 ± 3.4% upon treatment with SNEDDS. Early apoptosis stood at 24.6 ± 2.1% while late apoptosis was 34.1 ± 2.5%. Cellular uptake was evaluated with fluorescently labelled SNEDDS. It was determined by:

$$\text{Cellular uptake (\%)} = (\text{Cell-associated drug} / \text{Initial drug concentration}) \times 100$$

The optimised SNEDDS demonstrated $78.5 \pm 4.2\%$ cellular uptake post-treatment. Enhanced cellular uptake could increase intracellular levels of drugs. These results need to be validated using independent biological replicates.

DISCUSSION

From the results obtained, it is clear that SNEDDS could enhance the delivery performance of the anticancer drugs. The optimised formulation had small droplet size and low PDI, which are attributes that can enhance drug dispersion and increase the surface area. The optimised formulation had acceptable zeta potential in the process of storage. The drug loading and entrapment study revealed successful drug loading in the formulation. The in-vitro release pattern showed immediate release at the beginning, and sustained drug release afterwards. The behaviour exhibited here is expected to enhance drug availability in the body compared with the free drugs having poor solubility (Morakul et al., 2024). Moreover, cytotoxicity data showed that there was concentration-dependent decrease in the viability of cancer cells. The IC_{50} value reveals anticancer efficacy of the drug. The apoptosis studies demonstrated increased cell death due to SNEDDS treatment. Yet, these results need to be confirmed using independent biological samples. Additionally, there is a need to conduct statistical tests to see if the differences observed between the formulations are statistically significant. On the whole, these results indicate that SNEDDS are worth exploring in anticancer drug delivery. Yet, these laboratory results cannot be extrapolated to patients without animal and clinical studies. In other words, these results indicate that improvement in formulation features might lead to better cellular response. The results on the stability of the sample indicated small changes after storage. The drug's release must also be compared to that of the pure drug along with appropriate control formulations. In summary, the SNEDDS appears to be an encouraging platform for the delivery of anticancer drugs (Juarros Basterretxea et al., 2024). However, results obtained from the laboratory cannot be used to predict the success in the clinical setting. More investigations are needed in this field, which should consist of mechanism study, animal model, pharmacokinetic study, and toxicity test, among others. Replicates should also be done in order to validate the reproducibility.

CONCLUSION

There were many positive implications of SNEDDS in terms of increasing the effectiveness of anticancer drugs. First of all, SNEDDS offered appropriate physical stability and appropriate drug load and release rate and droplet size. Second, the results of cytotoxicity and apoptosis tests showed an increase in anticancer activity of the drugs. Nevertheless, it is necessary to confirm these results in terms of stability testing, animal experiments, pharmacokinetics, and clinical trials.

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