



## Application of Mobile Net Model to Assess the Phytoniosomes Loaded *Sonchus Maritimus* for Hepatocytes Targeting

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### Abstract

Lipid nanoparticles have received much attention owing to their applications as drug delivery systems. They can target specific tissues for delivering their contents and are secure as well as efficient. One kind of lipid nanoparticle known as niosomes is made up of non-ionic surfactants, which have been shown to be successful because of their long-term stability and biocompatibility. *Sonchus maritimus* is an important plant that exhibits various biological activities. The aim of this search is to use artificial intelligence in order to characterize the architecture of *Sonchus maritimus* loaded niosomes to target the affected liver tissue based on optical micrographs. It has been established that computerized examinations of the niosomes nanoparticle architecture were complex. A suggested approach automates the characterization of the niosome structure. Its foundation is the application of neural networks to the ability to recognize optical images of niosome nanomaterials and to determine the amount of *S. maritimus* extract contained in niosomes. The preliminary processing of the niosome nanostructure images is described, and the results of the use of neural networks to identify the niosomes' structural features are presented. The high accuracy of using neural networks to determine the niosomes' structural characteristics is demonstrated. The model has been developed for recognizing the images of nanostructures and determining the amount of the loaded extract in them. This investigation is important for determining the morphological characteristics of niosomes loaded plant extract and their differentiation from other niosomes.



This study sets a solid foundation for applying deep learning models in nanomedicine, with potential implications for enhancing precision in niosomes characterization.

**Keywords:** Niosomes, *Sonchus maritimus*, linoleic acid, Nanostructure, Artificial intelligence, Neural networks,

## 1. Introduction

Among the most attractive technologies of the twenty-first century is nanotechnology. It includes the capacity to manipulate, observe, measure, and produce components at the nanoscale level [1–3]. Due to the wide range of applications of nanoparticles in medicine fields, chemical engineering, catalytic processes and electronic sector, the industrial demand for them has increased recently [4,5]. One of the main uses of nanotechnology in the pharmaceutical sector is to improve drug delivery systems and create smart nanocarriers that can not only target the affected site and deliver specific biosubstances, while can also increase the solubility of drugs, shield therapeutic molecules from enzymatic damaging, and regulate medicines in the blood circulatory system [6]. Niosomes are among the vesicular nanocarriers that serve as drug delivery system and can contain either hydrophobic and hydrophilic molecules. They are capable of targeting diseased tissue while protecting adjacent healthy tissue [7]. In recent decades, phytotherapy has been useful for treating or preventing diseases, given that medicinal plants contain a group of chemicals with biological activities, such as polyphenols, flavonoids, and terpenes, which may intervene to solve the pathomechanism of diseases through their interaction together to increase the efficiency of each other or possess a synergistic effect, providing greater benefit from a single chemical component [8,9]. *Sonchus maritimus* is a species that belongs to a member of the Asteraceae family which is among the major plants that having medicinal and commercial significance [10,11]. *Sonchus maritimus* has shown efficacy against bacterial infections as well as antioxidant and anticancer features owing to its containing a variety of bioactive substances, including flavonoids, phenols, coumarins, steroids, fatty acids, and tocopherols [12,13]. The utilization of natural substances as medicines has attracted a lot of attention. In particular, fatty acids that are polyunsaturated, such as linoleic acid, have been found to be effective as bioactive lipids. It is metabolized in the liver, regulates energy metabolism, and maintains



metabolic stability. For that, linoleic acid is used to specially target liver affection [14,15]. Artificial intelligence (AI), computer image analysis, and machine learning have advanced rapidly, making it easier to extract quality features from products based on appearance, color, shape, and light spectrum [16]. Precising of object quality and recognition are made possible by modern digital tools and computer data processing methodologies [17]. Due to non-invasiveness and the growing computing capacity of computers, computer image analysis and convolutional neural networks has become among of the most widely used techniques nowadays, because of an important benefit over the labor-intensive and costly techniques currently in use [18,19]. This paper aimed to investigate the application of artificial intelligence technologies to recognize liver-targeted nanostructures of *Sonchus maritimus* loaded niosomes and determine the concentration of the plant extract in the nanocarrier.

## 2. Material and Methods

### 2.1. Collection of plant samples

Samples of *Sonchus maritimus* had been collected in November from Djamaa region in El-Oued, Algeria. Their classification was confirmed by botanist named "Pr. Halis Youcef" at the Center of Scientific and Technical Research on Arid Regions in Touggourt, Algeria. Following the wash of leaves with distilled water, they were let to completely dry at room temperature. Then, they were ground into a fine powder and kept at room temperature until use.

### 2.2. Preparation of aqueous extract

*Sonchus maritimus* extract was prepared using 100 ml of distilled water and 10 g of dry leaf powder. The mixture was left to macerate for twenty-four hours at room temperature and then filtered and dried on a stove at 50°C [20].

### 2.3. Preparation of niosomes

In order to produce bioconjugated niosomes by linoleic acid and loaded with *Sonchus maritimus* extract, 30 mg of cholesterol, 50 µg of linoleic acid, and 100 µg of tween 80 were dissolved in 100 mL of chloroform and ethanol at a 1:2 ratio in a circular-bottomed flask. The solvents were then removed using rotary evaporator (BUCHI R-210 Rotavapor ®,



Switzerland) in order to produce a thin layer on the flask wall. Subsequently, a liquid niosomal suspension including *S. maritimus* extract was produced by sonicating the layer for sixty minutes at 50°C in ultrasonic bath (Digital Ultrasonic Cleaner UC-230D, Spain) after dispersing it with 10 mL of the aqueous extract. After being allowed to develop at room temperature for the entire night, the phytoniosome mixture was refrigerated to get ready for additional research [21].

#### 2.4. Data Set Collection

The dataset comprises 850 photos of various niosomes. The samples were prepared on microscope slides. The data were photos which obtained using optical microscope (Optika B-293, Italy) on different magnifications of 10x, 40x, 100x at various angles with different light intensity. The data were captured using camera of iPhone XR and saved in HEIF/HEVC format at 1080 p at 240 fps. The dataset is divided into 5 groups based on the present of niosomes in the photos and the composition of loaded material in the niosomes

- Group 1 (None): Distilled water without niosomes
- Group 2 (NS-LA- SME-0): Niosomes –bioconjugated linoleic acid -loaded distilled water without *Sonchus maritimus* aqueous extract.
- Group 3 (NS-LA- SME-10): Niosomes -bioconjugated linoleic acid -loaded 10 mg/mL of *Sonchus maritimus* aqueous extract
- Group 4 (NS-LA- SME-50): Niosomes -bioconjugated linoleic acid -loaded 50 mg/mL of *Sonchus maritimus* aqueous extract
- Group 5 (NS-LA- SME-100): Niosomes -bioconjugated linoleic acid -loaded 100 mg/mL of *Sonchus maritimus* aqueous extract

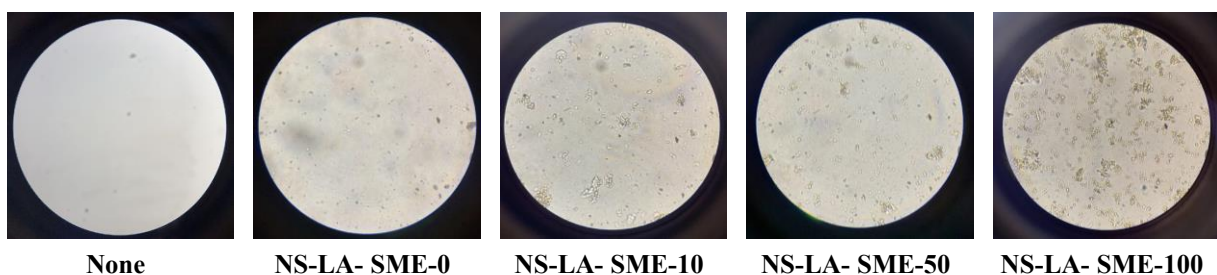


Figure 01: Phytoniosomes groups



## 2.5. Image Pre-processing

In seeking precise classification of phytoniosomes using deep learning techniques, the pre-processing of input images emerges as a pivotal phase. Involving a sequence of actions aimed at refining the quality and uniformity of images, thereby aiding in more efficient training and forecasting by the model. The preprocessing methodology adopted in this research includes Gaussian blurring, Contrast Limited Adaptive Histogram Equalization (CLAHE), Otsu's thresholding, and image resizing, followed by conversion to a format compatible with the MobileNet architecture.

The first stage entails employing Gaussian blur on the input images. This method employs a Gaussian kernel to soften the image, effectively diminishing noise and insignificant details that don't play a significant role in the classification task. By implementing this filter with a kernel size of (5, 5), we guarantee that the vital structures within the phytoniosomes images remain intact while reducing unnecessary information. This step is vital for bolstering the resilience of subsequent image analysis procedures, especially in settings with fluctuating lighting conditions or where samples might display slight physical differences.

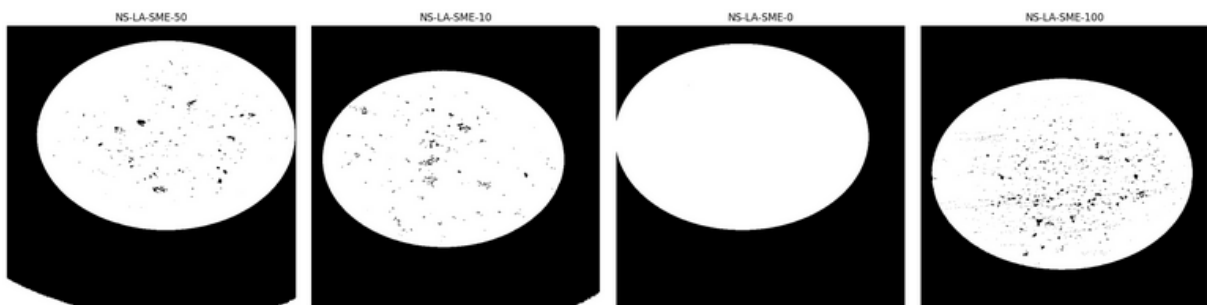
After reducing noise, the subsequent step focuses on boosting the contrast of the images. For this purpose, CLAHE is utilized, targeting the grayscale rendition of the blurred image. Unlike conventional histogram equalization methods, CLAHE restricts the amplification of contrast to avoid excessive enhancement of noise in areas of the image with relatively uniform characteristics. This is accomplished by dividing the image into contextual sections and applying histogram equalization to each section independently, employing a clip limit of 2.0 and a tile grid size of (8, 8). The outcome is a harmonized improvement in the visual clarity and definition of the niosomes, thereby facilitating more precise edge detection and feature extraction in subsequent stages.

Following contrast improvement, Otsu's technique transforms the image into a binary form, separating the foreground (particles of phytoniosomes) from the background. This thresholding method identifies the best threshold value by minimizing intra-class variance in



the image, thereby accurately isolating the pertinent features from their surroundings. This binary depiction streamlines the recognition and categorization of niosomes by concentrating on the particles' shape and arrangement.

The final stages of the pre-processing procedure involve adjusting the size of the binary image to a uniform dimension of 640x640 pixels, guaranteeing uniformity across the dataset and adhering to the input size specifications of the MobileNet model. To adhere to the model's requirement of three-channel input, the grayscale image is replicated across three channels, mimicking the structure of an RGB image without introducing additional color data. This standardized input configuration is essential for the MobileNet architecture to efficiently and precisely process the images. Through careful execution of each pre-processing step, the study ensures that the phytoniosomes images are optimally prepared for subsequent application of deep learning models. As illustrated in Figure 2, this preparation enhances the model's capacity to discern significant patterns within the data, thereby enhancing the overall dependability and accuracy of the niosomes classification results.



**Figure 2:** Phytoniosomes photo in the four groups after pre-processing

## 2.6. MobileNet training process

The primary dataset was methodically divided into three distinct subsets: training, validation, and test. This three-way split is essential for evaluating the model's learning effectiveness, its ability to handle new data, and its overall performance in a fair, unbiased assessment. Table 1 provides an overview of the dataset distribution, promoting transparency in the experimental setup of the model.



**Table 1:** Data Splits

Data Split	Description	Percentage & Size
Training subset	Allows the model training, where it learns the distinctions between different classes.	80% - 544 Image
Validation	Offers an initial assessment of the model's capacity for generalization.	50% of the 20% - 68 Image
Test	Assesses the model's ultimate performance on data it has not encountered before.	50% of the 20% - 68 Image

To optimize the training process, the data were converted into TensorFlow datasets, utilizing the platform's effective data management and processing features. This transformation allows for advanced batching, shuffling, and prefetching operations, improving computational efficiency. The specifications used for this conversion are outlined in Table 2.

**Table 2:** Converting the data into TensorFlow datasets

Parameter	Functionality	Specified Value
buffer_size	Ensuring the dataset's shuffling capability is essential for reducing any bias introduced by the order of the data during the learning process.	Length of Dataset
batch_size	Controls the number of data samples processed per iteration by the model, striking a balance between computational workload and learning granularity.	32
prefetch_buffer	Pre-fetches data batches to accelerate data processing, optimizing pipeline throughput.	AUTOTUNE

The MobileNetV2 architecture, recognized for its computational efficiency and strong feature extraction abilities, was chosen for the classification task in this study. The incorporation of this model, customized with a specialized top layer designed for phytoniosomes classification, highlights the innovative methodology of the research. Detailed configuration specifics are provided in Table 3.



**Table 3:** MobileNetV2 Configurations

Configuration Element	Description
Base Model	MobileNetV2 was initialized with ImageNet weights and then adjusted to exclude the top layer, which acts as the basis for feature extraction.
GlobalAveragePooling2D	Compresses the feature maps into a single vector per image, simplifying the model's interpretive process.
Dense Layer	It consists of 1024 neurons activated by ReLU, assigned with the duty of learning intricate associations within the data.
Dropout Layer	Incorporates a dropout rate of 50% to alleviate overfitting by randomly excluding neurons during training.
Output Layer	Concludes with a softmax-activated layer, producing a probabilistic distribution across the Phytoniosomes categories.

The training regimen relied on the Adam optimizer, chosen for its adaptive learning rate functionality, enabling subtle adjustments to the model. Early stopping, based on validation loss performance, was implemented methodically to prevent overfitting. Training and evaluation metrics, vital for assessing the model's effectiveness, are outlined in Table 4.

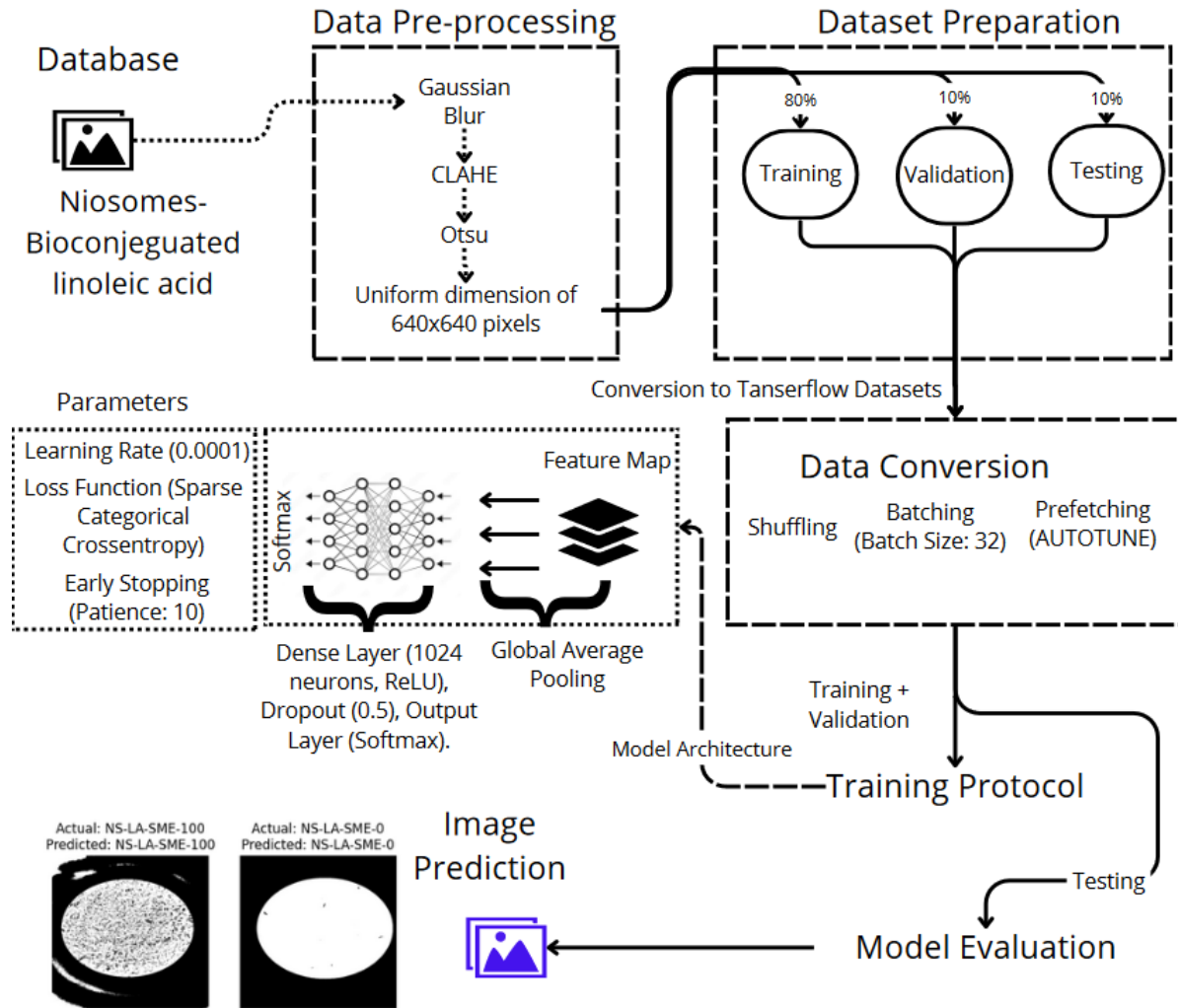
**Table 4:** Parameters and Metrics

Parameters/Metrics	Description
Optimizer	Adam was selected due to its effectiveness in managing sparse gradients and its capability to adjust the learning rate adaptively.
Learning Rate	Set at 0.0001, this value ensures a gradual convergence, mitigating the risk of overshooting the minimum of the loss function.
Loss Function	Sparse Categorical Crossentropy was employed, aligning with the multi-class nature of the Niosomes-Bioconjugated linoleic acid classification task.
Evaluation Metrics	The model's performance is evaluated using accuracy, offering a direct assessment of classification success rates.

The meticulous approach taken in model training and architecture design highlights the study's dedication to precision and reproducibility. By adhering to these methodological standards, the research makes a valuable contribution to the growing field of niosomes classification, laying the groundwork for future investigations into AI-driven pharmaceutical



advancements.



**Figure 03:** MobileNet model training and architecture for classification in a graphical format

### 3. Results

Our deep learning model, utilizing the MobileNetV2 architecture via transfer learning, underwent a comprehensive training process spanning 65 epochs. At the outset of training, we observed a loss of 1.3614 and an accuracy of 39.95%, as expected given the model's initial untrained state. Over the course of training, there was a notable enhancement in the model's accuracy, with the training accuracy reaching 86.12% by the final epoch. Validation accuracy began at 51.47% and exhibited fluctuations, reflecting the model's adaptation to the

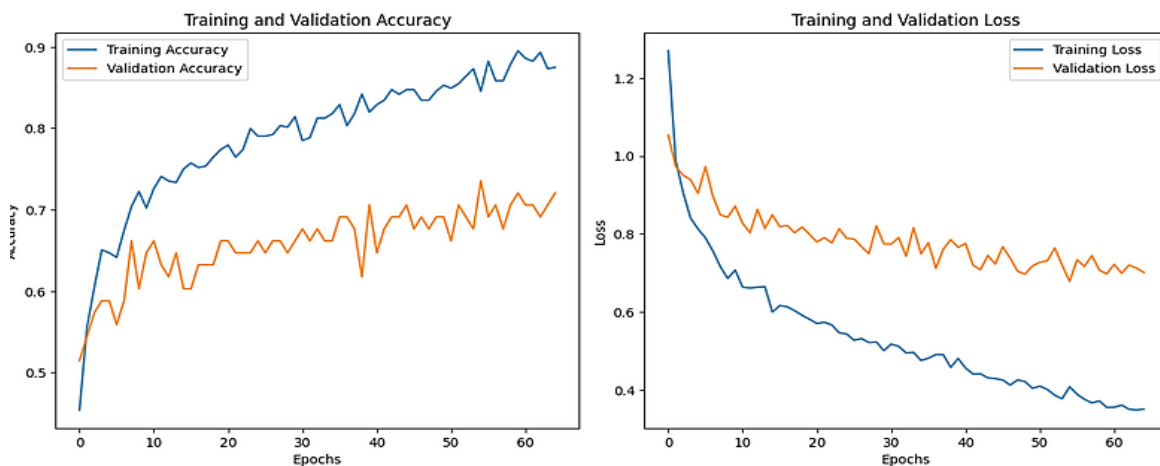


validation dataset, ultimately peaking at 73.53% in the 55th epoch. Correspondingly, validation loss decreased over time, aside from sporadic increases typical during the optimization process (refer to Table 5).

**Table 5:** Model Training and Validation Performance

Epoch	Training Loss	Training Accuracy	Validation Loss	Validation Accuracy
1	1.3614	39.95%	1.0534	51.47%
...	...	...	...	...
55	0.4182	84.42%	0.6788	73.53%

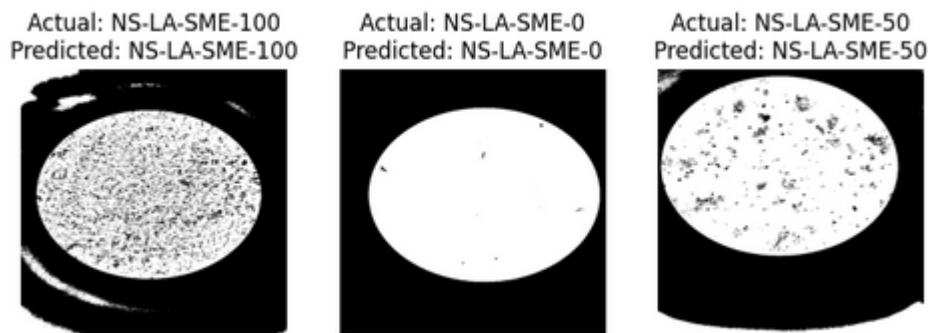
The final evaluation of the model on the test set, which was held out from the training process, revealed an accuracy of 77.94% and a loss of 0.4816. This performance benchmark underscores the model's ability to generalize effectively and demonstrates its robustness when encountering unseen data. The learning curves (refer to Fig.4) offer insights into the model's learning trajectory. The training accuracy demonstrates a consistent increase as the model learns from the data. In contrast, validation accuracy closely follows, indicating effective generalization rather than mere memorization of the training data. Similarly, both training and validation loss metrics decrease over time, aligning with the increases in accuracy.





**Figure 04:** Training and Validation Accuracy and Loss Curves

Visual inspection of the model's predictions provides a qualitative understanding of its performance. Figure 5 showcases a subset of images from the test set, displaying both the model's predicted class labels and the actual labels. This visual examination unveils instances of correct classifications, such as accurately predicting 'NS-LA-SME-100' as 'NS-LA-SME-100'. These examples illustrate the model's strengths while also identifying areas where its classification abilities can be refined further.



**Figure 05:** Sample Predictive Performance on Test Samples

The instances of accurate predictions validate the model's efficacy in classifying phytoniosomes. However, the misclassifications provide valuable insights into potential confusion between classes, emphasizing the necessity for further refinement of the model's training to augment its discriminative ability, particularly for closely related classes.

#### 4. Discussion

Niosomes are a type of carrier system that encapsulate the medicine and variety of bioactive chemicals in a vesicle with cholesterol acting as a stabilizer and non-ionic surfactants forming a bilayer structure. This amphiphilic bilayer architecture traps the medicine inside and allows it to pass through biological membranes, increasing the drug's therapeutic efficiency even though it has a poor water solubility [22]. When cytotoxic medications are administered systemically, they may initially act on healthy tissues before reaching the targeted tissues, which can result in their cytotoxicity. Overall, pharmacokinetic



characteristics of 70% of pharmaceuticals produced worldwide are subpar in vivo [23]. In order to address this issue, nanoparticle-based drug delivery systems have been created to deliver therapeutic substances more precisely and effectively. This prevents the effects of administered drugs from damaging nearby organs, which would otherwise occur if the drugs were in their free form. Drug delivery systems have been researched and developed over the past few years for the treatment of a variety of diseases associated with different organs, such as the liver, heart, and brain [24]. As an evidences, an experimental in vivo study on rats, used *Sonchus maritimus* loaded niosomes, as drug delivery system to target affected liver by administration of high-fructose diet, when linoleic acid act for targeting especially liver and *Sonchus maritimus* extract act as medication [25]. In our study, the excellent accuracy on the test set and the learning curves during training demonstrate the model's capacity to learn and generalize from the given data. The model was able to recognize the phytoniosomes, and to predict the concentration of the loaded *S. maritimus* extract inside of the niosomes. Previous studies used artificial intelligence to control various features and factors related to nanocarriers drug delivery systems and their synthesis. Researchers employed artificial neural networks in a study to identify the parameters controlling niosomes' size of particles and entrapment efficiency in nanoparticles made of polylactide (PLA) and polyethylene glycol (PEG) [26]. Kalantary, *et al.*, utilized artificial network and multiple regression in order to predict the diameter of natural/synthetic nanofibers in medical applications [27]. Previous studies depend on encapsulation efficiency to investigate niosomal system which can load therapeutic substances. The quantity of medication enclosed in these drug system may be divided by the total quantity of medication used in the manufacturing process to determine the efficiency of entrapment in niosomal vesicles [26,28]. Shahiwala *et al.* employed a machine learning technique to create optimal medication compositions. At 93.76% and 91.79% for drug entrapment percentage and particle size prediction, respectively, the network had the highest prediction accuracy [29].

## Conclusion

In summary, the trained MobileNetV2 model demonstrates promising performance in classifying niosomes loaded *Sonchus maritimus* aqueous extract. The results reveal the



model's ability to learn and generalize from the provided data, as evidenced by the high accuracy on the test set and the learning curves during training. The visual predictions further validate the model's practical capabilities while guiding future improvements. This study sets a solid foundation for applying deep learning models in nanomedicine, with potential implications for enhancing precision in phytoniosomes characterization.

### **Credit authors statement**

S.C., and A.N.A. Writing original draft. S.D. Conceptualization, Supervision, & editing.

### **Declaration of competing interest**

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

### **Data availability**

<https://www.kaggle.com/code/abidmohamednadhiri/niosomes-mobilenet-classification/notebook>

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Not applicable' for that section.

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