A Machine Learning Analysis for Identifying Relationships between Liposomal Characteristics and Anticancer Drugs

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Introduction

Liposomes hold a pivotal role in nanomedicine, because of the presence of two different compartments; the aqueous and the lipidic, which allow for the trapping of both hydrophilic and hydrophobic molecules. This structure gives liposomes the advantage of improved pharmacokinetic qualities of the medicine they are encapsulating, decreased systemic toxicity, longer circulation durations, and targeted drug delivery in tumor areas [1]. Meanwhile in the digital era, machine learning (ML) algorithms have played a critical role in improving predictions of biological, physical, chemical, and toxicological impacts, by uncovering patterns within datasets [2].

Objective

This study aims to identify relationships and correlations among the physicochemical parameters of the liposomes, with a particular focus on size, zeta potential, polydispersity index (PDI), and encapsulation efficiency (EE). By collecting quantitative and qualitative data from PubMed between 2022 and 2023, analyzing them, and finally, extracting valuable information, this study seeks to uncover relationships and correlations among these parameters.

Methodology

• The articles were collected from PubMed using the keywords: liposomes and cancer. The initial number of papers was 603, but after the exclusion criteria [e.g. not about an active pharmaceutical ingredient (API)] the number was finalized to 130, with 313 formulations. The data from the papers were categorized into qualitative (i.e. Liposome preparation technique) and quantitative [i.e. Mean Size (nm)].

• Python was chosen as the programming language for data analysis. Among the libraries that were implemented were: pandas, numpy, seaborn and sklearn, for data manipulation, numerical computations, data visualizations and ML algorithm implementation, respectively [3].

• The data files were transformed into python dataframes and data cleaning was followed. Each column was examined separately for their missing or NaN values. For the quantitative data, the NaN values were replaced with the mean of the column, after using descriptive statistics to examine the data. Then, a univariate and a bivariate analysis was conducted, as well as a correlation analysis and a hypothesis testing. Both qualitative and quantitative data were explored for hidden patterns using visualizations.

• The three ML techniques that were employed next were: the k-means clustering method, the agglomerative hierarchical clustering method, and the Principal Component Analysis (PCA) technique. For the first two, the results were evaluated with the silhouette score, while for the PCA the reconstruction error was computed [4].

Results

• K-means clustering exhibited a higher evaluation score than the agglomerative clustering. The clustering suggests that the larger the mean size, the higher the PDI will be.

• Also, the EE decreases as the mean size increases (p-value<0.01). On the other hand, the EE appears to be rather high with mean sizes around 500–600 nm.

• The mean PDI, out of the four parameters of the quantitative data, shows a weaker correlation with the other three, according to the PCA.

• The biplot (Figure 1) also indicates a positive association between the EE and the zeta potential.

• Research is focused on breast cancer, with doxorubicin being the primary active substance, followed by docetaxel.

• The thin-film hydration process is the most often utilized method for producing liposome formulations and the ethanol injection method is second.

• In certain studies, the ethanol injection method outperformed the thin film hydration method in terms of EE (breast cancer, liver cancer, colorectal cancer, brain cancer, lung cancer, cervical cancer) (Figure 2).

Conclusion

• This research represents a step toward a time when liposome-based medicines will be essential in the fight against cancer [5,6].

• With this information in hand, the formulation scientists can design and develop a liposomal nanomedicine with the desired physicochemical characteristics and added value to the therapeutic outcome [7].

• Given the findings and the significance of research in cancer therapy, studies should concentrate more on the physicochemical properties of liposomes.

• Considering the large number of APIs studied, it may be inferred that improving how the liposomes

reach their goal with the encapsulated API is less important than focusing on a substance real therapeutic effects.

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Figures

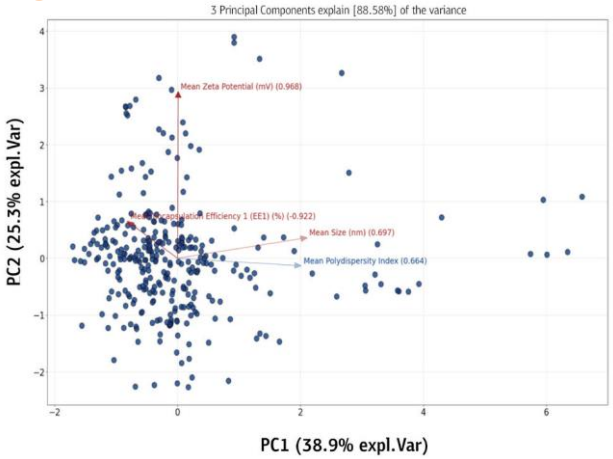

Figure 1. Principal component analysis biplot for the liposomes features.

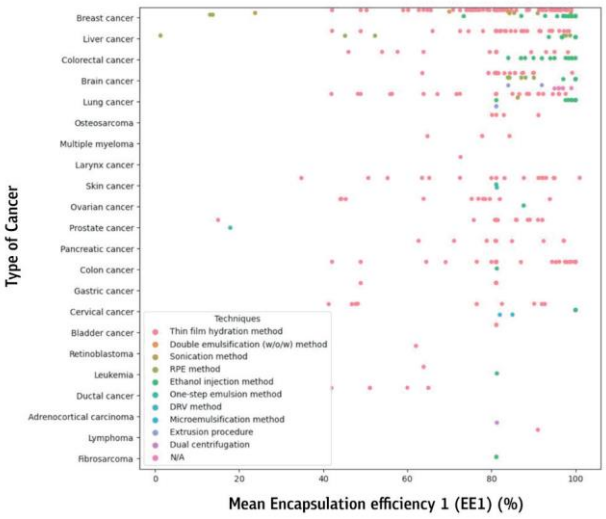

Figure 2. Type of Cancer - Mean EE plot, color coded by the liposome preparation technique.