NTA2022

2nd International Conference on
Nanotechnology: Theory and Applications,
Cairo, 19 – 21 Dec., 2022

Ref. 056

Revelation of the microsponges' predominant fabrication parameters and influence on *in vitro* biological activities of Adapalene

Rania M. Yehia[1*], Mahmoud H. Teaima[2], Dalia A. Attia[1], Mohamed M. Elmazar[3] and Mohamed A. El-Nabarawi[2]

[1]Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, The British University in Egypt (BUE), El-Sherouk City, Cairo, Egypt.

[2]Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Cairo University, Cairo, Egypt.

[3]Department of Pharmacology and Toxicology, Faculty of Pharmacy, The British University in Egypt (BUE), El-Sherouk City, Cairo, Egypt.

Presented by: Rania M. Yehia, Rania.yehia@bue.edu.eg

KEYWORDS

Plackett-Burman, anticancer, antibacterial, UVA irradiation.

SHORT SUMMARY

Adapalene (ADA), a third-generation retinoid that have been widely used in the treatment of acne together with being recently exploited as an anticancer drug. However, ADA is frequently accompanied by momentous topical side effects that affect the treatment process and patient's compliance. Therefore, there is an urgent need for a carrier system that is capable of delivering ADA in a manner that minimizes the associated side effects. The microsponges (MS) are proposed in the present study to be investigated for Adapalene delivery due to their well-known merits in drug delivery.

Herein, the first part of the present investigation was to explore the parameters that affect the formulation of ADA –MS. Secondly, the investigation of MS system contribution to the in vitro biological activities of Adapalene. Proficient in vitro performance of the ADA loaded microsponges was assured. By depression in the IC_{50} values by 5.26 and 4.3 folds, compared with the ADA alone against the cancerous cell lines A431 and M10. Also, the improvement of the cell viability of HFB-4 cell-line exposed to UVA irradiation by 14 % to 43 % compared with pure ADA. Lastly, the reduction of the MIC against P. acnes. Hence, these results offer the prospect that MS could be privileged as carrier system for topical drug delivery.

EXTENDED ABSTRACT

AIM OF WORK:

The focus of the study was to scrutinize the microsponges (MS) as a carrier system for delivery of a model drug (Adapalene). In order to evaluate the parameters that influence the microsponges' characteristics, Plackett-Burman approach was utilized. Furthermore, our golden objective was to study the contribution of the MS system on the *in vitro* biological activities of ADA.

METHODOLOGY:

Experimental screening design, preparation and characterization of microsponges

Variables that affect the formulation were screened utilizing Plackett-Burman design.The chosen independent variables were volume of organic phase (A) either 5 or 20 ml, sonication time (B) 5 or 15 minutes, stirring speed (C) either 500 or 1500 rpm, drug percent (D) 50% or 80%, polymer type (E) Eudragit RS100 or Ethyl Cellulose, emulsifier concentration (F) 0.1% or 0.5%, and lastly method of organic phase addition (G) either portionwise or dropwise. The dependent variables were entrapment efficiency (E.E.%), production yield (P.Y.%), particle size (P.S.) and morphology (using SEM imaging). Furthermore, the quasi-emulsion solvent diffusion method was used to prepare the MS [1].

In vitro biological activity assays for selected prepared ADA-MS

The biological effects of ADA loaded into selected microsponges formulae; using either Ethyl cellulose as polymer (ADA-MS-EC) or using Eudragit RS100 as polymer (ADA-MS-EUD) were

investigated in comparison with ADA in free form. They were the cytotoxic effects on epidermoid carcinoma (A431) and melanoma cell lines (M10) the photoprotection effect on normal cell line (HFB-4) after being subjected to UVA irradiation, and the antimicrobial activity against *P. acnes via* determination of the minimum inhibitory concentration [2].

RESULTS:

The ADA loaded microsponges were successfully fabricated (Figure 1). The E.E.% varied between 38.48% and 99.76%, the P.Y% from 33.2% to 93.14%. As for P.S. it ranged from 14.97 µm to 162.6 µm and the particles morphology had different grades of homogeneity. In addition, as presented in Figure 2, the study indicated that the drug percent, polymer type and surfactant concentration have the key significant effect on E.E.% and P.Y.%, while, the drug percent, stirring speed and volume of organic phase have had a significant effect on P.S. and their morphology.

Moreover, the selected formulae ADA-MS ADA-MS-EC and ADA-MS-EUD, showed high efficiency in in vitro biological assays as demonstrated in Figures 3,4 & 5.

Acknowledgements

The authors gratefully acknowledge Dr. Yasmin M Attia, Associate Professor of Pharmacology and Toxicology, Faculty of Pharmacy, The British University in Egypt, for performing the UVA irradiation and cell viability assay. The authors would also like to thank Khaled A Abdelrahman, Microbiology Department, Faculty of Pharmacy, The British University in Egypt, for the execution of the MIC assay.

References

[1] Jadhav N, Patel V, Mungekar S, Bhamare G, Karpe M, Kadams V (2013) Microsponge Delivery System: An updated review, current status and future prospects. Journal of Scientific and Innovative Research 2:1097–1110

[2] Rusu A, Tanase C, Pascu GA, Todoran N (2020) Recent advances regarding the therapeutic potential of adapalene. Pharmaceuticals. https://doi.org/10.3390/ph13090217

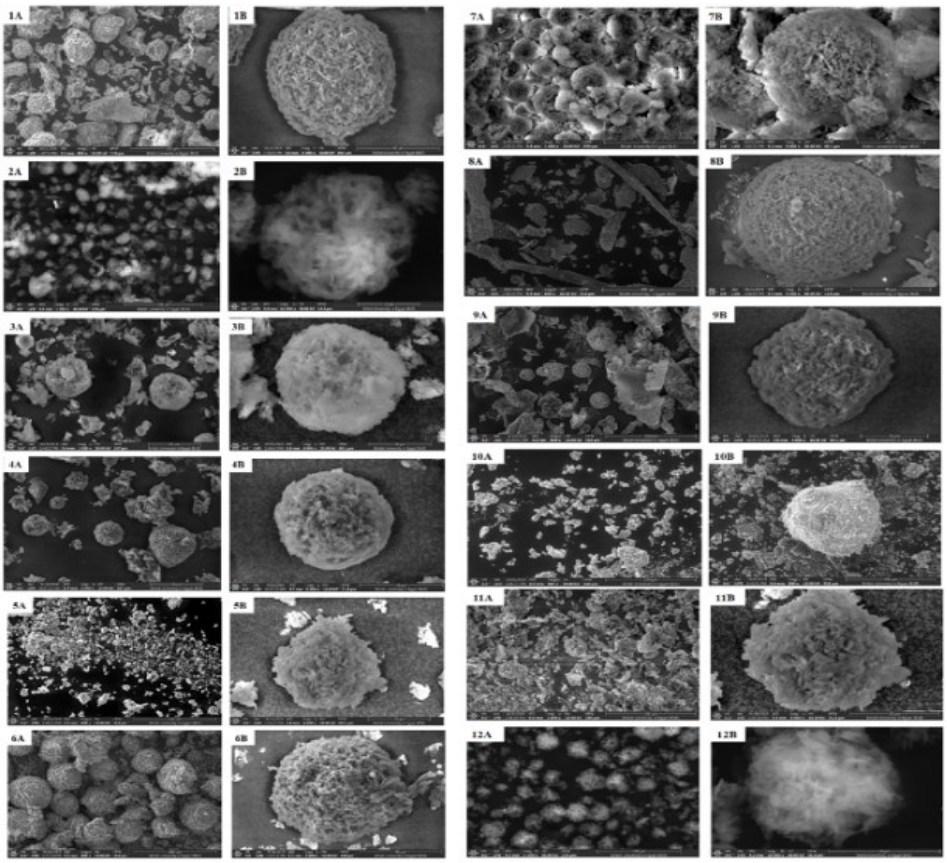

Figure 1 The SEM images of F1 to F12 where A: image of the field and B: image of a single microsponge particle.

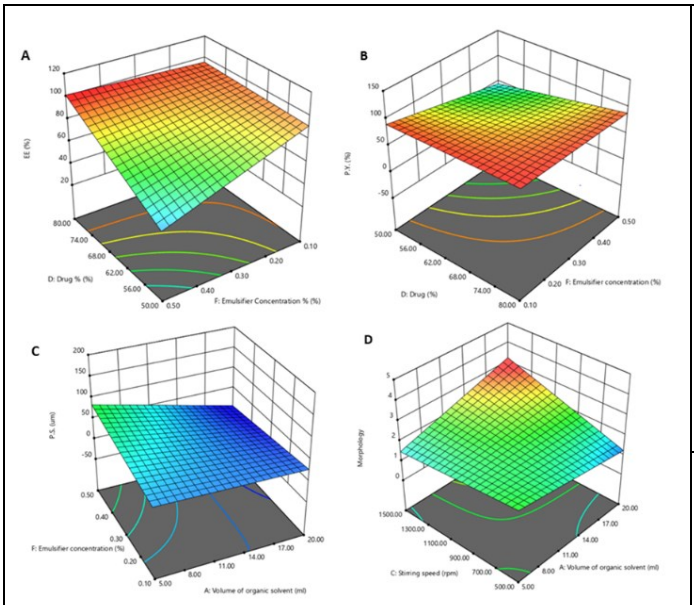

Figure 2 Three-dimensional (3D) of Plackett Burman design generated response surface plots of: (A) entrapment efficiency percentages in terms of DF, (B) production yield percentage in terms of DF, (C) particle size in terms of AF, and (D) morphology in terms of AC. The change in colour from blue-green-red indicates increase in response value

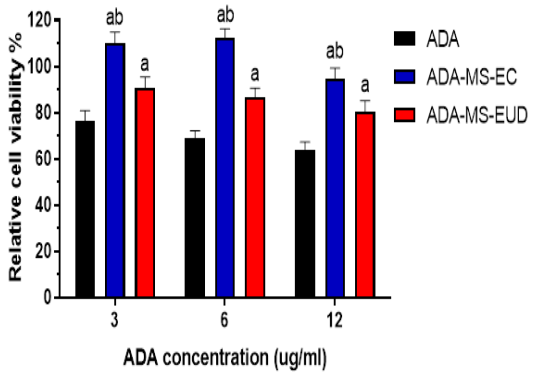

Figure 4 Cell viability assay after UVA irradiation and exposure to different concentrations of Adapalene in form of the free ADA, ADA-MS-EC and ADA-MS-EUD against HFB-4 cell line. Results were compared for each concentration using one-way ANOVA followed by Tukey's post hoc test. a: $p < 0.0005$ compared with respective ADA relative cell viability percent, b: $p < 0.0001$compared with respective ADA-MS-EUD relative cell viability percent

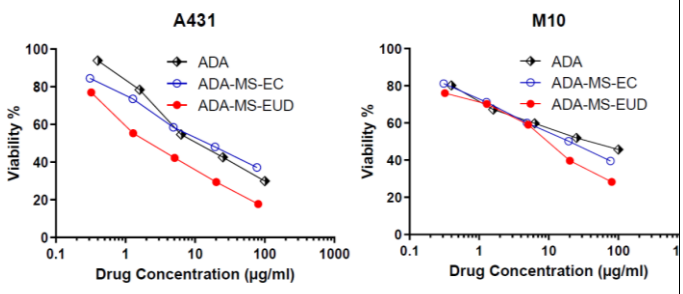

Figure 3 Cytotoxicity profile of the free ADA, ADA-MS-EC and ADA-MS-EUD against A431 and M10 cell lines

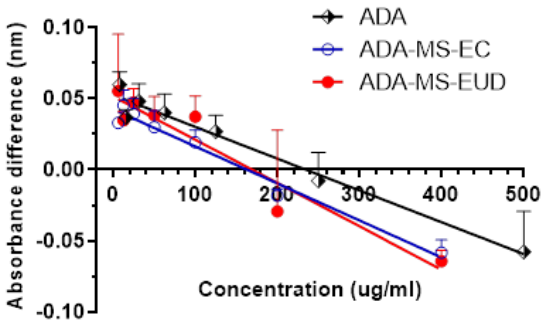

Figure 5 Minimum inhibitory concentration determination after exposure to different concentrations of ADA, ADA-MS-EC and ADA-MS-EUD against P. acne

.

.