Preparation and evaluation of mucoadhesive resveratrol microbeads using thiolated alginate for intrapocket delivery

Abeer Ahmed Kassem [a,b], *Ragwa Mohamed Farid* [c], *Doaa Ahmed Elsayed Issa* [d,e], *Doaa Said Khalil* [f], *Mona Yehia Abd-El-Razzak* [g], *Hussein Ibrahim Saudi* [g], *Heba Mohamed Eltokhey* [h], *Enas Arafa El-zamarany* [i]

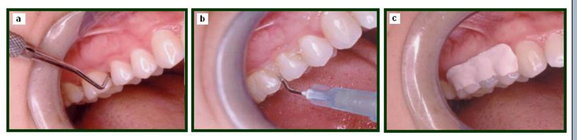
[a] Department of Pharmaceutical Sciences, Faculty of Pharmacy, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia, [b] Department of Pharmaceutics, Faculty of Pharmacy, Alexandria University, Alexandria, Egypt, [c] Department of Pharmaceutics, Faculty of Pharmacy and Drug Manufacturing, Pharos University in Alexandria, Alexandria, Egypt, [d] Department of Pharmaceutical Sciences, Faculty of Pharmacy, Beirut Arab University, Beirut, Lebanon, [e] Department of Pharmaceutical chemistry, Faculty of Pharmacy, Alexandria University, Alexandria, Egypt, [f] Department of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of Dentistry, Pharos University in Alexandria, Alexandria, Egypt, [g] Department of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of Dentistry, Tanta University, Tanta, Egypt , [h] Department of Oral Biology, Faculty of Dentistry, Tanta University, Tanta, Egypt, [i] Department of Clinical Pathology, Faculty of Medicine, Tanta University, Tanta, Egypt

Introduction

Resveratrol (Res) is a polyphenolic phytoalexin naturally existing in many plants, e.g. grapes. It has a promising therapeutic efficacy towards treatment of periodontal disease *in vitro*. However, it shows poor oral bioavailability due to rapid metabolism in liver together with the entero-hepatic cycle. Subgingival application of Res ensures high intrasalcular concentration and thus avoiding systemic side effects and ensuring better patient compliance

Aim of the work

This work aims to develop Res microbeads with strong mucoadhesion using thiolated alginate (TA) for local treatment of periodontal pockets



Methodology

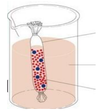
Synthesis: The thiolated alginate (TA) was synthesized by esterification of hydroxyl groups of sodium alginate (A) with carboxyl group of thioglycolic acid. The resultant product was characterized by IR and DSC.

A and A/TA Res microbeads with different ratios: 1:1, 2:1, 3:1 and 4:1, were prepared by orifice-ionotropic gelation method using 10% Calcium chloride solution

The mucoadhesive properties of both A and A/TA 1:1 microbeads containing Res were evaluated by ex vivo wash-off method

%EE was determined by dissolving microbeads in of 5% Sodium citrate solution and then drug was extracted with Ethanol

***In vitro* drug release study** was performed in 30% ethanol in Sørenson phosphate buffer pH 6.6 using cellophane dialysis bag



Swelling-erosion behavior study was done by placing 10 mg microbeads in a sieve and dipping it into a beaker containing 20 mL of pre-warmed buffer at 37 ±0.5°C in incubator. Sieves removed at specified time intervals, blotted with filter paper and weighed.

% Swelling was calculated

The morphology of A and TA and drug loaded A and TA microbeads were investigated using scanning electron microscope (SEM)

Results

FT-IR results: Appearance of -SH stretch band of mercaptans at 2592.89 cm^{-1} in TA confirming its formation

DSC results: A decrease in the endothermic transition temperature and heat of fusion of A was observed upon thiolation

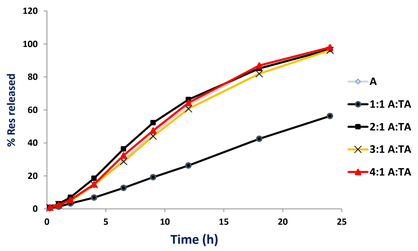
***Ex vivo* mucoadhesion study** using Drug-loaded A and A/TA 1:1 microbeads expressed as % Remaining microbeads after specified time intervals

Time (min)	A ±SD	A/TA 1:1 ±SD
5	95.6 ±3.85	99.6 ±0.89
15	69.6±6.54	88.4 ±5.73
30	42.8±16.59	73.2 ±9.76
45	14.4±9.1	51.2 ±19.52
60	2±1.79	26 ±15.23
70	0±0	16 ±15.3

%EE for all formulations

Formulation Code	Polymer (s) ratio A:TA	% EE±SD
A	1:0	100.36 ±1.45
A:TA 1:1	1:1	83.72 ±7.87
A:TA 2:1	2:1	104.54 ±9.82
A:TA 3:1	3:1	104.35 ±10.13
A:TA 4:1	4:1	98.01 ±9.29

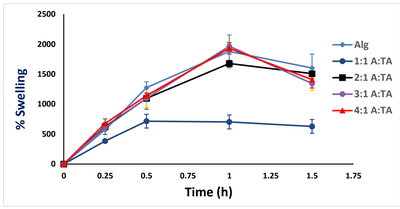
***In vitro* drug release & release kinetics**



A significant reduction in release rate could be observed for TA rich formulation A/TA 1:1, compared to all other formulations those did not exhibit significant difference to each other. The drug release kinetics was non- Fickian transport super case II, in which the dominant mechanism for drug transport is polymer relaxation as the gels swell

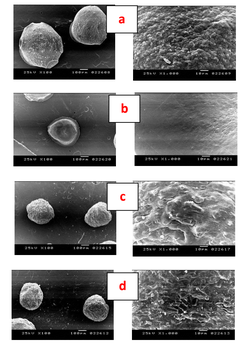
Results (Cont.)

Swelling behavior



All A rich formulations exhibited increased % swelling during the first hour compared to TA rich formulation A/TA 1:1 after which erosion has started

SEM micrographs



(a) Placebo A, (b) Placebo A/TA 1:1, (c) Drug-loaded A microbeads and (d) Drug-loaded A/TA 1:1 microbeads

Conclusion

Strong mucoadhesive microbeads were successfully prepared by thiolated sodium alginate. It could be exploited for intrapocket delivery of Res for local treatment of periodontal pockets

References

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Contact information

Abeer Ahmed Kassem: Department of Pharmaceutical Sciences, Faculty of Pharmacy, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia

Department of Pharmaceutics, Faculty of Pharmacy, Alexandria University, Egypt

Email: abeerkassem2002@gmail.com

Tel.: +201223608155 - +966580014010