Macedonian pharmaceutical bulletin, 69 (Suppl 1) 95 - 96 (2023)
Online ISSN 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2023.69.03.046
Short communication

Dermal acrylic and silicone patches – the effect of liquid additives

Małgorzata Sznitowska[1], Marzena Jamrógiewicz[2], Bartosz Maciejewski[1], Barbara Mikolaszek[1], Justyna Strankowska[3], Krystyna Pieńkowska[2], Joanna Dłabiszewska[1], Sandra Dybowska[1], Damian Rosłonowski[1]

[1] *Department of Pharmaceutical Technology, Medical University of Gdansk, Hallera Street 107, 80-416 Gdańsk, Poland*
[2] *Physical Chemistry Department, Medical University of Gdansk, Hallera Street 107, 80-416 Gdańsk, Poland*
[3] *Institute of Experimental Physics, Faculty of Mathematics, Physics and Informatics, University of Gdańsk, Wita Stwosza 57, 80-308 Gdańsk, Poland*

Introduction

Transdermal adhesive patches may contain liquid excipients which help to disperse the active pharmaceutical ingredient (API) in the polymer matrix, but also modify internal matrix structure and the release rate and skin absorption of API. Moreover, application properties of the product can be influenced, such as adhesion, skin tolerance or occlusion. The aim of the study was to evaluate the effects of liquid components of dermal patches on their biopharmaceutical, morphological and application properties (Mikolaszek et al., 2022). Different types of polymers forming the matrix were tested, classified as silicones (SSA) or acrylates (DT) and liquid excipients were: silicone oil (SO), polyoxyethylene glycol (PEG), propylene glycol (GP), isopropyl myristate (MIP) and triethyl citrate (TEC), triacetin (TA).

Materials and methods

Preparation of the patches

The silicone patches (SSA) were prepared by mixing two components with polymerization catalysts (LiveoTM Soft Skin Adhesive MG 7-9850 DuPont, Brussels, Belgium). Acrylic patches DT were prepared by casting and evaporation method using DuroTak® polymers: 87-4098 (DT8), 87-2852 (DT2) Henkel, Brussels, Belgium). Polyethylene (PE) membrane (Esselte, Warsaw, Poland) was used as a backing layer for DT and silicone elastic film – for SSA. Placebo patches and containing indomethacin (IND, 5% w/w) were prepared. Liquid components (10% w/w, alone or with IND) were mixed with the polymers in a planetary mixer Thinky assuring good homogeneity of the mass.

Adhesion test in vitro

The test was performed according to the USP method "Peel adhesion test" using TA.XT Plus texture analyzer (Stable Micro Systems, Godalming, UK). The patch was peeled from the glass plate under 90° angle. Based on the acquired force-distance curve, the initial peel force, as well as mean peel force were evaluated.

Oxygen permeation

100 cm^2 patches were examined with coulometric method according to ASTM F1927-98.

In vivo performance

Placebo patches were applied to the arms of volunteers for 24 h. The experiment was performed according to the permission of the Bioethical Commission. The force of detachment was measured using a Texture analyzer and the removed patches were observed under microscope. Moreover, Transepidermal Water Loss (TEWL) was measured. The irritation test was performed by Eurofins Dermscan (Gdansk, Poland).

In vitro drug release

*malgorzata.sznitowska@gumed.edu.pl

The experiments were carried out for the patches with IND using a pharmacopoeial paddle over disk apparatus and phosphate buffer pH 7.4. Concentration of IND in the acceptor medium was assayed with HPLC/UV.

Before the experiment and after 48-96 h exposure to the dissolution medium the patches were analyzed: microscopically (SEM and Raman microscopy), by FTIR spectroscopy and wet and dry weight was measured to evaluate swelling and erosion.

Results and discussion

Microscopic analysis of the placebo formulations showed good compatibility in acrylate-based samples, except for compositions containing SO. The silicone-based patches showed very limited compatibility exhibiting no signs of phase separation only with MIP and SO. Besides, most of liquid excipients, except SO and GP, caused almost complete loss of adhesiveness in SSA patches. On the other hand, IND appeared to slightly improve the peel parameters previously reduced by liquids.

TEC, TA and PEG caused increase in the initial peel force of DT2 placebo compositions, but the effect of MIP and GP was opposite. In DT8-based formulations with PEG a reduction of peel adhesion was observed.

No irritation in vivo was observed after application of the patches without additives or with MIP. Additional tests were performed with SSA patches and significant irritation was observed in the case of SSA-PG patch, while SSA-SO was the best tolerated. Due to different backing membranes there was a large difference in oxygen permeability through SSA and DT patches (43688 and 603 $cm^3/m^2/24h$), however large inter-individual deviations in TEWL values were observed in vivo and no conclusion was obtained regarding the relationship between type of the patch and this parameter.

Irrespective of the liquid added IND was dissolved in DT type patches but remained suspended in SSA patches. The liquid additives promoted the drug release with the most pronounced effect of MIP both in SSA and DT. In Fig. 1 the effect of PEG, GP, MIP and TEC on the release of IND from the acrylic patch is presented. Modification of the SSA matrices with MIP or SO affected the drug diffusion even in more visible way than observed for DT.

In Table 1 changes in the mass of the acrylic patches immersed in the dissolution medium are presented. It can be seen that the promotion of in vitro drug release by MIP can be explained by neither better swelling nor by special erosion of the patch.

After the release test the patches were dried and were tested for adhesiveness. It was found that the adhesive properties were significantly reduced. The Raman maps showed much lower fraction of IND visible on the patch surface after the release test. Addition of the liquid excipients resulted in the increase of the dissolved fraction of IND within the polymeric matrix. FTIR spectra were compatible with the drug release test since the absence of IND bands was more evident in the patches containing liquid additives.

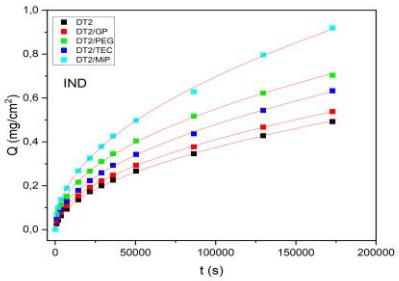

Fig. 1. Release of IND from DT2 patches with and without liquid additives.

Table 1. Mass increase (swelling) and dry residue (after "erosion") [%] of DT2 patches with IND

Additive	Swelling		Erosion
	3h	96h	96h
GP	108.0±9.5	114.3±14.9	80.6±20.6
MIP	108.5±9.6	120.0±7.2	98.5±8.4
PEG	112.0±6.5	153.3±7.4	96.9±7.7

Conclusion

The results indicate that liquid excipients can be used to intentionally modify the properties of the patches. Higher compatibility with liquid excipients, as well as better adhesive properties were exhibited by the patches based on acrylates. Unfortunately, even if the liquid excipient is apparently compatible with the polymer and promotes drug release, the adhesive properties can still be significantly reduced.

Ackowledgements: This research was supported by Polish National Science Centre (NCN, grant 2018/29/B/NZ7/01111). The polymers were provided free of charge by the Henkel and DuPont.

References

Mikolaszek B, Jamrógiewicz M, Mojsiewicz-Pieńkowska K, Sznitowska M., 2022. Microscopic and Spectroscopic Imaging and Thermal Analysis of Acrylates, Silicones and Active Pharmaceutical Ingredients in Adhesive. Polymers doi:10.3390/polym14142888