

COMPETITION

P1.82

Thermosensitive polymers as a component for synthesize of thermoregulated transdermal patch with dandelion extracts (*Taraxacum Officinale*)

Tanaguzov T. M., Bekenova A. K., Glazhdinova M. M., Begimova G. U.
Kazakh National Medical University named after S. D. Asfendiyarov, Almaty, Kazakhstan

Abstract

Nowadays there are different ways of delivering drugs. But most of them have their own disadvantages. One of the interesting way of drug delivering is transdermal patches (TP). Drug diffuses straightaway to the bloodstream avoiding the gastrointestinal tract, thus not affecting the organs and having less side effects. For controlled drug diffusion thermosensitive polymers can be used. Poly-2-ethyl-2-oxazoline showed properties of thermosensitive polymer that could be applied for synthesize of thermoregulated transdermal patch. Physicochemical properties showed different results depending on ratio of substances. But this component is hard to be obtained because of its price. There are also a lot of other thermosensitive polymers, such as poly(N-isopropylacrylamide) (PNIPAM) or triblock poly(ethylene glycol)-poly(ϵ -caprolactone)-poly(ethylene glycol), which even have already been used for synthesize of thermosensitive gel. Work is aimed at finding a better recipe of synthesize of thermosensitive transdermal patch filled with dandelion extract as a main drug.

Introduction

In modern medicine delivering of the drug plays a big role in effectiveness of the drug. So development of better way of the delivering is a task for pharmaceutical companies. Transdermal patches are one of gaining popularity way to deliver the drug. Transdermal delivery system is an attractive option because the drug can bypass gastrointestinal tract and so do no harm to the organs. There are different types of transdermal patches and structures for regulating drug diffusion. In this work thermoregulation topic is covered. Thermosensitive substances are being used already for a long time in pharmaceutical businesses. Poly(2-oxazolines) examples of such substances. Poly 2-ethyl-2-oxazoline (PEtOx) [1, 2] is a relatively new material with a big potential. In this work PEtOx is mainly used due to its relative novelty.

Dandelion has a lot of different substances. One of them is phlorizin – new and effective antimicrobial agent that dilutes in ethanol.

Goals of this work

- Create thermosensitive patch with LCST (lower critical solution temperature) at -40°C so it will match with human skin temperature
- Add phlorizin as a main drug
- Test properties of the patch

Materials

Polyvinyl alcohol (PVA), ethanol 96%, poly 2-ethyl-2-oxazoline (Sigma-Aldrich, 372846-100G, average Mw $\sim 50,000$, PDI 3-4), gellan gum (Sigma-Aldrich), chitosan (Sigma-Aldrich), sodium alginate, sodium chloride, calcium chloride, glutaraldehyde (Sigma-Aldrich), phosphoric acid, acetic acid, food coloring, phlorizin (Sigma-Aldrich).

Patch synthesis

No	PVA	Sodium alginate	Chitosan	Gellan gum	CaCl ₂	Glutaraldehyde	PEtOx	Phosphoric acid	Acetic acid
1	40%								
2		1.25%			2.5%		0.65%		
3			3%						
4			3%				3%	3%	5%
5				2%	2.5%		2%		
6				2%	5%		2%		

Everywhere the solvent was water. Only films with gellan gum and CaCl₂ were successful. Different concentrations were tried, but 2% of gellan gives the best physical properties. According to the literature, 2% of PEtOx is an optimal choice for thermosensitive property. Substances were diluted together in water, 70°C for 10 minutes, then room temperature, 750 rpm. Afterwards the solution was poured into a Petri dish. Now there are 2 ways to finish patch: 1 – leave for 20 minutes for patch to form a bit, then add calcium chloride solution as a linking agent. Leave again for 24 hours for calcium to fully react.

2 – leave for 24 hours for it to completely dry out and only then add calcium chloride again for 24 hours.

1st way is thinner and for neater formation.

2nd way is sticky, had a form, but was too soft so the

Adding of phlorizin

Phlorizin is a non-polar substance so we diluted it in 96% ethanol. According to literature [4] water content of gellan gum patch can be replaced with ethanol therefore phlorizin will go into the patch as well. 1% solution of phlorizin were poured in 3 Petri dishes with patch. As a control group 3 more patches were put in ethanol with no phlorizin.

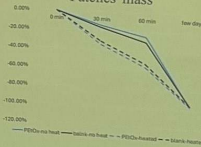
Patches mass' difference



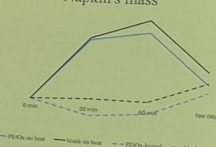
Thermosensitive test

To test the thermal sensitivity, experiments were carried out based on studying the release of food dye (active substance) from a sample of the patch and the diffusion of the dye into the napkin, followed by measurements of the change in mass and external assessment of the color of the napkin. Experiments were carried out on a heated surface (-40°C) and at room temperature to compare thermal sensitivity. To confirm PEtOx influence patch with no thermosensitive agent was also tested.

Patches' mass

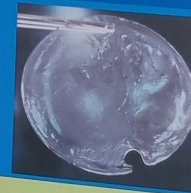


Napkin's mass



Results and discussion

- PEtOx is decreasing exiting content from the patch in both heated and with no heat situations. It is assumed that LCST of this patch is over than 40°C therefore PEtOx forms bonds with content of the patch and make it harder to release it. Color saturation almost didn't differ.
- Phlorizin penetration into the patch is confirmed.
- Patch is durable, flexible. Thickness is 0.376 mm on average if it is dried first.



Work was supported by the Ministry of Education and Science of the Republic of Kazakhstan (AP 19679386).