Creation and assessment of herbal transdermal patches based on Arnica essential oil for the relief of pain

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Abstract:

When applied to the skin, a transdermal patch is an adhesive pad containing medication that releases the active component gradually over several hours to days. It has been discovered that medications from herbal sources can be added to transdermal medication patches for increased effectiveness. Thus, transdermal drug delivery system (TDDS) provides an improved delivery method with higher patient compliance. In the present work we tried to formulate and evaluate Arnica Montana herbal patches. *Arnica montana* (arnica) contains a variety of terpenoids and has mostly been used in the treatment of sprains and bruises but is also used in cosmetics. *Arnica montana*, a yellow flowering plant found native to northwest America, Mexico, Siberia, and parts of Europe, is also known as *leopard's bane*, *mountain tobacco*, or *wolfsbane*.

Keywords: Transdermal drug delivery, medicated patches, herbal agents,Transdermal patches, Arnica Montana.

1. INTRODUCTION:

The term "transdermal drug delivery systems" (TDDS) describes formulations designed to distribute a prescribed medication through a patient's skin in an appropriate amount, guaranteeing the of the medication at a therapeutic dosage into the body.
It is crucial to take into account all of the biophysical, morphological, and physicochemical characteristics of human skin in order to transfer medicinal chemicals through it and produce systemic effects. Transdermal medication administration is superior to injectables and oral methods because it avoids the first-pass metabolism and increases patient compliance [1]In order to avoid nausea and vomiting, the FDA authorized the first transdermal system in 1979. Verification of the topical medication.Monitoring the patient's clinical reaction to the prescribed medication therapy, measuring blood levels, and detecting drug and metabolite excretion in urine are all ways to determine absorption [2]. permeate an ethylene vinyl acetate membrane with rate control. A variety of medications, including nicotine, estradiol, fentanyl, clonidine, scopolamine (hyoscine),and combining norethisterone acetate with estradiol. The type of pharmacological therapy will determine the precise location of the patch administration [3].

1.1 Advantages of TDDS:

- Transdermal administration guarantees a sustained and continuous penetration of a material over a prolonged length of time, preventing first-pass metabolism [4]
- Boost adherence from patients.
- It doesn't impede the stomach or intestines' liquid flow[5].
- Sustains consistent and constant blood levels, providing control over an extended period [6,7]
- Lower drug plasma concentration levels.
- Use medication options with short half-lives and low therapeutic indices to minimize drug swings in plasma levels.

1.2 Disadvantages of TDDS:

- It was not possible to get high drug levels in blood or plasma [8].
- It is impossible to create medications with large molecular sizes [9].
- The potential for irritation at the application site [10].
- It is uncomfortable to wear.
- It could not be cost-effective.
- The skin barrier differs from person to person and might even alter over time within an individual.

1.3 Plant profile [26-29]:

Numerous traditional cultures have developed, recorded, and finally institutionalized their indigenous knowledge into systems of medicine like ayurveda, siddha, unani, and other Indian systems.It is a member of the Asteraceae family, which also contains daisies and sunflowers. For generations, arnica has been a part of herbal therapy due to its well-known therapeutic qualities. This is a summary of Arnica's traits, applications, and safety measures:

1.4 Characteristics:

- **Appearance:** Arnica plants normally reach a height of 20 to 60 cm. Their blooms are brilliant yellow and resemble daisies, with ray florets around a center disk.
- **Leaves:** Oval-shaped, hairy, and opposite in form are the leaves.
- **Habitat:** Most usually found in hilly areas, meadows, and forest clearings, arnica favors damp, nutrient-rich soils.

2. Material and methods:

2.1 Collection of *Arnica oil [11];*

We used a 20-mesh sieve to crush the dried leaves into smaller pieces, and then a 40-mesh sieve to further refine the process. I eliminated waxy substances by subjecting around 500 grammes of the powdered material to continual extraction in a Soxhlet machine with petroleum ether for 24 hours. I then used distilled water to do an extraction that lasted 72 hours. Evaporation of the water after 72 hours produced a basic extract with a concentration of 7.4 percent by volume and weight. The extract underwent dehydration in an oven with a tight lid. Represent in figure 1.

Figure.1 Soxhlet apparatus

2.2 Transdermal Patch [12-19]:

Using three different ratios (1:4, 1:6, and 1:8), six samples of Arnica oil were used to make transdermal patches that included a medication and two different polymers. We heated the given amount of polymers in a water bath after immersing them in the exact amount of water. The next step was to add the extract in a measured quantity to the batter and stir vigorously until getting a uniform texture. What next was the addition of the exact amounts of ethanol and permeation enhancers. In each of the six batches, the quantity of extract was the same. We placed the finished mixture in a Petri dish and let it dry out for 24 hours at room temperature. After that, we used a knife to remove the patches from the Petri plates, and then we put them in a desiccator to keep them.Mention in tanle no.1.

Table.1 Formula for Transdermal patches

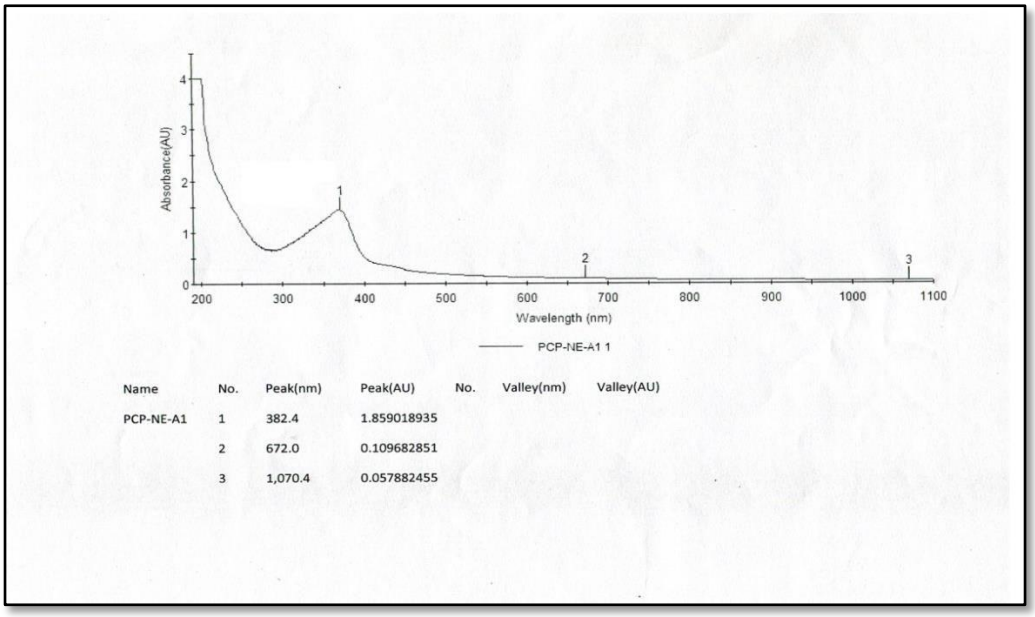
Ingredients	TP1	TP2	TP3	TS4	TS5	TS6
Arnica Oil (ml)	40	40	40	40	40	40
Pectin (mg)	160	240	320	-	-	-
Sodium Alginate (mg)	-	-	-	160	240	320
DMSO (ml)	0.3	0.3	0.3	0.3	0.3	0.3
Glycerin (ml)	0.3	0.3	0.3	0.3	0.3	0.3
Water (q.s.)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

2.3 Creating a Calibration Curve for Arnica Oil Extract [20-25]:

The stock solution had a concentration of 1 mg/ml after diluting 100 ml of Arnica oil extract (AE) with distilled water from an original amount of 100 mg. After adding buffer to 1 milliliter of this concentrated solution, the final amount was 10 milliliters. We took volumes ranging from half a milliliter to three milliliters and mixed them with distilled water to get a final amount of ten milliliters. The results showed that the concentrations ranged from 5 to 50 µg/ml. We used a UV spectrometer to measure the absorbance at 382 nm, which allowed us to build a calibration curve.

3. Result and discussion:

Arnica oil's peak absorption (λ max) is the range of wavelengths where it shows the most absorption (Figure 2).



Name	No.	Peak(nm)	Peak(AU)	No.	Valley(nm)	Valley(AU)
PCP-NE-A1	1	382.4	1.859018935			
	2	672.0	0.109682851			
	3	1,070.4	0.057882455			

Figure 2 shows the highest absorption value (λ max) of the Arnica oil water extract.

3.1 Standard Curve values of *Arnica oil (Figure 3):*

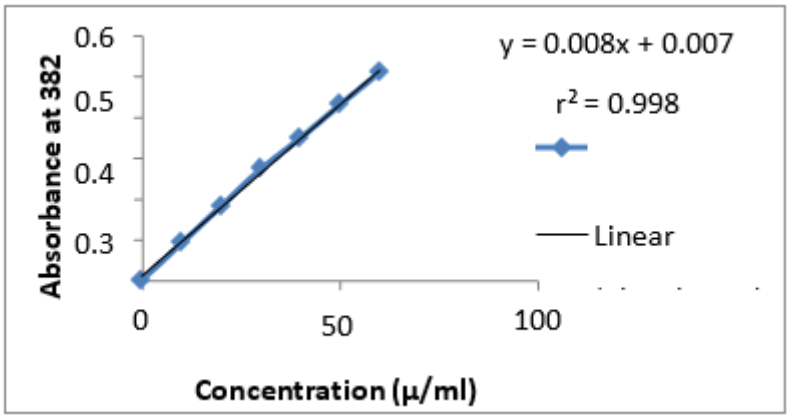


Fig No.3: calibration Curve

3.2 In vitro drug diffusion study:

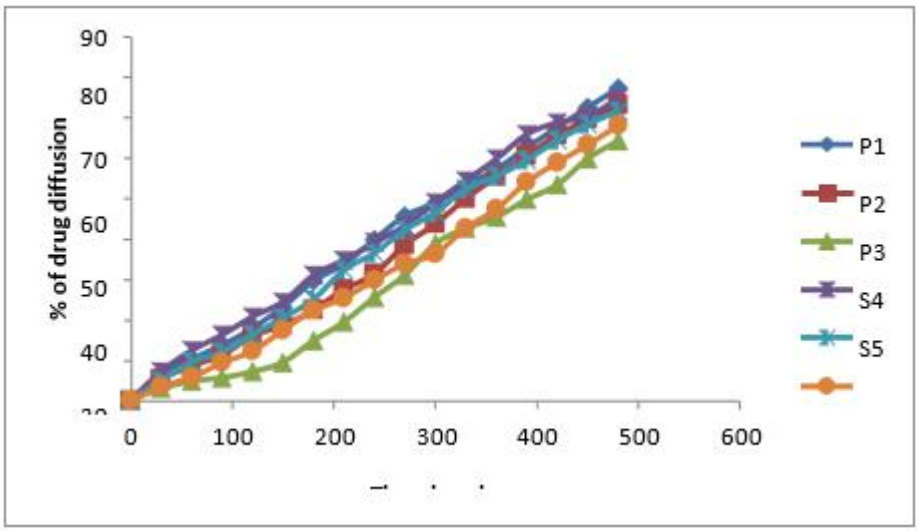


Fig No.4: Study of drug dispersion in an artificial environment

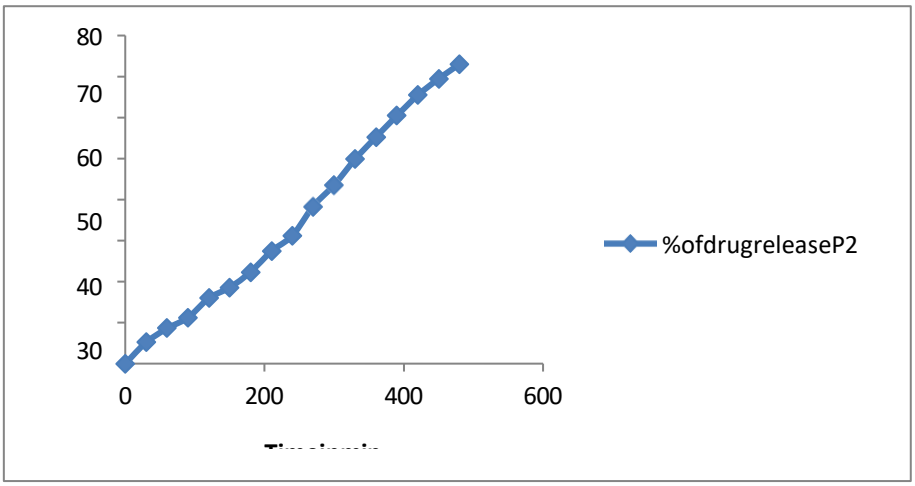


Fig No.5: The drug dispersion profile of P2 was studied using in vitro methods

We used the solvent casting approach to manufacture six patches that contain anarnica oil for transdermal administration. Thin, transparent, smooth, stable, and highly permeability patches were the result of an optimization process that included modifying several parameters, including drug-polymer ratios and permeability enhancers.There were no peaks or expanding bands found in the FTIR analysis of the drug, excipients, or formulations, proving that they are compatible. We found that P2 and S5 were the best formulations after looking at their physical and chemical qualities and how effectively they diffused in a controlled setting.

Adding 0.3 cc of glycerin, a plasticizer, made the patch more flexible without significantly altering its diffusion characteristics. However, stiffness occurred with an overabundance of glycerin. The plasticizer also helped the polymer soften and the patches to form.

The patches were tested on a number of characteristics, such as their capacity to absorb moisture, the amount of moisture, their thickness, their resistance to folding, the concentration of the medicine, their elongation, and their adhesive force. P2 and S5 performed really well across the board. The fact that the medication content remains constant across different formulations is evidence of uniform drug distribution.

Conclusion:

He development of arnica transdermal patches represents a promising advancement in natural pain relief and anti-inflammatory treatment. By harnessing the therapeutic properties of arnica, which has long been used in traditional medicine for bruising, muscle pain, and swelling, these patches offer a convenient and targeted method of delivery. Transdermal patches provide sustained release of arnica's active compounds, potentially enhancing its efficacy while minimizing systemic side effects associated with oral administration. In conclusion, arnica transdermal patches could serve as an effective alternative for individuals seeking natural pain management solutions. However, further research and clinical trials are necessary to fully validate their safety, efficacy, and optimal usage in diverse patient populations. Continued development and refinement of these patches may lead to broader acceptance and integration into mainstream therapeutic options.

Future prospect:

The future prospects for the development of **Arnica montana** transdermal patches are promising, driven by the growing demand for natural and alternative therapies. As more people seek natural and holistic approaches to pain management and inflammation, **Arnica montana** transdermal patches are well-positioned to meet this demand. The trend towards avoiding synthetic drugs with potential side effects will likely drive continued interest in arnica-based products. Ongoing research in transdermal drug delivery systems may lead to more efficient and effective patches. Innovations such as improved skin permeation techniques, enhanced adhesive formulations, and controlled-release mechanisms could optimize the delivery of **Arnica montana**'s active compounds, increasing the patches' therapeutic efficacy. Future studies focused on the clinical efficacy and safety of **Arnica montana** transdermal patches will be crucial for their wider adoption. Positive results from well-designed clinical trials could lead to greater acceptance by healthcare providers and integration into standard treatment protocols.

Refrences:

1. Allen LV, Popovich NG, Howard C. Ansel. Pharmaceutical dosage forms and drug delivery systems, 8th Edn. New Delhi: Wolter Kluwer Publishers; 2005. p. 298–9.
2. Kumar P, Sankar C, Mishra B. Delivery of macromolecules through skin. *Indian Pharm*. 2004;5(3):7–17.
3. Hanbali OA, Khan HMS, Sarfraz M, Arafat M, Ijaz S, Hameed A, et al. Transdermal patches: Design and current approaches to painless drug delivery. *Acta Pharm*. 2019;69(2):197–15.
4. Zhang Y, Yu J, Kahkoska AR,Wang J, Buse JB, Gu Z, et al. Advances in transdermal insulin delivery. *Adv Drug Deliv Rev*. 2019;139:51–70. doi:10.1016/j.addr.2018.12.006.

5. De Vos P, Faas MM, Spasojevic M, Sikkema J. Encapsulation for preservation of functionality and targeted delivery of bioactive food components. *Int Dairy J*. 2010;20(4):292–302.
6. Heifer P, Shultz TR. Coupled feedback loops maintain synaptic long- term potentiation: A computational model of PKMzeta synthesis and AMPA receptor trafficking. *PLoS Comput Biol*. 2018;14(5):1006147.doi:10.1371/journal.pcbi.1006147.
7. Barry B. Transdermal drug delivery. In: Aulton E, editor. The science of dosage forms design, 2nd edn. . Churchill Livingstone, New York: Harcourt publishers; 2002. p. 499–533.
8. Williams AC, Barry BW. Penetration enhancers. *Adv Drug Deliv Rev*. 2012;64(5):128–18.
9. Ng LC, Gupta M. Transdermal drug delivery systems in diabetes management: A review. *Asian J Pharm Sci*. 2020;15(1):13–25. doi:10.1016/j.ajps.2019.04.006.
10. Gupta J, Thakur A, Thakur S. Transdermal drug delivery system of Metformin Hydrogen Chloride using Two Different Polymeric Combinations. *Int J Heal Biol Sci*. 2019;2(4):1–5.
11. **Sayan Bhattacharjee, S. NagalakshmiS. Shanmuganathan**. Formulation characterization and in-vitro diffusion studies ofherbal extract loaded mucoadhesive buccal patches *Indian journal of pharmaceutical sciences research,* 2014, vol:5(11): 4965-497.
12. Danby SG. Biological Variation in Skin Barrier Function: From A (Atopic Dermatitis) to X (Xerosis). *Curr Probl Dermatol*. 2016;49:47–60. doi:10.1159/000441545.
13. Menon GK. New insights into skin structure: scratching the surface. *Adv Drug Deliv Rev*. 2002;54(1):3–17.
14. Benson HA, Watkinson AC. Topical and Transdermal Drug Delivery: Principles and Practice. Hoboken, NJ, USA: Wiley; 2012.
15. Suh H, Shin J, Kim Y. Microneedle Patches for Vaccine Delivery. *Clin Exp Vaccine Res*. 2014;3(1):42–9.
16. Walters KA. Dermatological and Transdermal Formulations. Boca Raton, FL, USA: CRC Press; 2002.
17. Alexander A, Dwivedi S, Giri TK, Saraf S, Saraf S, Tripathi DK, et al. Approaches for Breaking the Barriers of Drug Permeation through Transdermal Drug Delivery. *J Control Release*. 2012;164(1):26–40.
18. Wilson R, Waugh A, Grant A. Anatomy and physiology in health and illness. 9th Edn. Churchill Livingstone; 2001. p. 363–6.
19. Kumar D, Sharma N, Rana AC, Agarwal G, Bhat ZA. A review: transdermal drug delivery system: tools for novel drug delivery system. *Int J Drug Dev Res*. 2011;3(3):70–84.
20. **Ansel.H.C, Loyd.A.V, Popovich.N.G**, Pharmaceutical dosage forms and drug delivery systems, Transdermal drug delivery system introduction . Lippincott Williams and Willkins publication.Seventh edition, Section8 : 646-668.
21. **Tiwary AK, Sapra B and Jain S** innovations intransdermaldrugdelivery: formulations and techniques recent patentson drug delivery & formulation. *journal of pharmaceutical research*2007 vol:3(1): 23-36.
22. **Syeda Ayesha Fathima, Shireen Begum, Syeda Saniya Fatima**.Transdermal Drug Delivery System, *International Journal of Pharmaceutical and Clinical Research* 2017,vol 9(1): 35-43.

23. **Singh J,Tripathy KT and Sakia TR**.Effect of penetration enhancers on the in vitro transport of ephedrine through rat skin and human epidermis from matrix based transdermal formulations. *Journal of Drug Delivery International Pharmaceutical research*.1993,vol:19(11):1623-1628.
24. **Pravin Chinchole, Sagar Savale and Kamlesh Wadile**, Novel Approach On Transdermal Drug Delivery System [Tdds] *International journal of pharamaceutical sciences.*2016, Vol:5(4), 932-958.
25. **Debjit Bhowmik, K.Rao.Pusupoleti, S.Duraivel, KP.Sampath Kumar**. Recent Approaches inTransdermal Drug Delivery System.*The pharma innovation-journal* 2013 vol.2(3): 99.
26. immerman HJ. Unconventional drugs. Miscellaneous drugs and diagnostic chemicals. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999: pp. 731-4.*(Expert review of hepatotoxicity published in 1999; several herbal medications are discussed, but not Arnica montana).*
27. Liu LU, Schiano TD. Hepatotoxicity of herbal medicines, vitamins and natural hepatotoxins. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 2nd ed. New York: Informa Healthcare USA, 2007, pp. 733-54.*(Review of hepatotoxicity of herbal and dietary supplements [HDS] published in 2007; no mention of Arnica montana).*
28. *Arnica montana*. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 43-47.*(Compilation of short monographs on herbal medications and dietary supplements).*
29. Hörmann HP, Korting HC. Evidence for the efficacy and safety of topical herbal drugs in dermatology: Part I: Anti-inflammatory agents. Phytomedicine. 1994;1:161–71. [PubMed].