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Importance of Adhesive Performance of Transdermal Drug Delivery Systems

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1. Editorial

Transdermal drug delivery systems (TDDS) are adhesive patches which deliver the therapeutic agent through the skin at a controlled rate to the systemic circulation and to the target organs **(1)**. These systems provide more convenient and effective therapy compared with the oral and parenteral ways. The most important advantages are improved bioavailability with the avoidance of 'first pass' effect of liver and the enzymes in digestive system. Improved patient compliance is provided by controlled delivery of drugs, hence constant blood levels and reduced dosing frequency compared to the conventional oral dosage forms is obtained. Additionally, in some cases like adverse effects the patient has the advantage of removing the patch immediately and also being a non-invasive application makes TDDS more acceptable and accessible for wide range of patient populations **(2,3)**. The advantages of transdermal applications for the patient could be achieved with a well-conceived formulation including polymers, penetration enhancers, rate controlling membranes, adhesives, impermeable backings and also release liners **(4)**.

Effective drug therapy with the transdermal formulations can only be obtained with the whole contact between the patch and the skin surface. Lack of adhesion is a critical factor that changes the delivery and absorption process of the drug of a transdermal formulation that is designed to contact with the whole surface area. After the application onto the appropriate skin area, the patch must adhere completely to the skin surface and then drug partition between TDDS and the skin begins and the process of drug permeation proceeds with the whole delivery surface for prescribed time period. If the contact between TDDS and the skin decreases or disappears in the cases of patch lift or patch falling off, drug absorption will diminish and as a result, patients will have improper drug doses causing therapeutic failure. Only a constant patch/skin complete contact over the entire application period allows a convenient delivery and absorption of the drug **(5,6)**. Also, the patches that have poor adhesion must be replaced more often to complete the prescription time period and consequently that increases the treatment cost. Besides the inappropriate dosing and payment issues, there is also a problem about safety according to the

lack of adhesion. There is risk for children about having accidental contact with the fallen patches. There are also reports about death and other serious medical problems according to the accidental exposition of patches transferred from an adult to children or fallen down from an adult **(7)**. Adhesion problems can also be seen according to the usage in different environmental conditions like; heat, cold, sweating, swimming and showering. Lack of quality caused conditions like inability of removing the release liner properly also results in different sticking problems **(8)**. Reasons for early replacement of fentanyl transdermal patches of which were administered to cancer patients were carried out in a survey. It was pointed out that unless there was any physiological, pharmacological or environmental reason for explaining the early replacement of patches, the problem was about skin adhesion and that was mimicking end-of-dosage failure **(9)**.

A well- designed transdermal formulation with maximum efficacy and reliability, also have to carry out the requirements for adhesivity which is a critical factor for determining the therapeutic effect and the patient compliance as well as other compendial and non-compendial in vitro tests for characterization of the TDDS. There are three main in vitro techniques for evaluating the in vitro adhesive performance of the formulations; peel adhesion, shear strength and probe tack. Peel adhesion, is measurement of the required force to remove the adhesive once it has been attached tightly to a surface. Shear strength is a measure of the cohesive strength, performing the ability of the adhesive to peel away from the substrate without leaving a residue **(7,10)**.

The probe tack tests are used to measure the force required to separate the probe from the adhesive surface after applying a light pressure. Tack is measured as the maximum value of the force required to break the bond after a short period of contact with the surface (8). A probe is pushed forward with a light pressure and predefined speed into contact with the adhesive surface and then pulled back at a certain speed. The force required to break the bond after a short time period of contact is plotted in a force–time diagram. Texture Analyzer is an instrument used to measure the peak force at separation, the area under the curve, and the displacement upon de-bonding **(7,11)**. An example of a probe tack test was described in our previous study. Adhesive performance of transdermal therapeutic systems (TTS) containing captopril together with synthetic and pH independent polymers, Eudragit RL 100 and RS 100 was evaluated by using TA. XT plus Texture Analyser (Stable Micro Systems, UK, Godalming, Surrey). Results indicated that the mechanical properties of the formulations were suitable to be used as a transdermal patch. The optimum firmly attached to the skin, indicating good adhesion properties for clinical use **(12)**.

In conclusion, as lack of adhesion is a critical factor that changes the delivery and absorption process of the drug of a transdermal formulation, the patch must adhere completely to the skin surface. If the contact between the TDDS and the skin decreases or disappears in the cases of patch lift or patch falling off, drug absorption will diminish and as a result, patients will have improper drug doses causing therapeutic failure. Only a constant patch/skin complete contact over the entire application period allows a convenient delivery and absorption of the drug. Besides the inappropriate dosing and payment issues, there is also a problem about safety according to the lack of adhesion. When developing a new patch formulation, adhesivity should be taken into consideration as one of the most important characterization parameter.

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