6.1.7. Folding endurance

A film is taken and folded repeatedly at a point continuously, till, it breaks. The total number of times the patch could be folded at the same place without breaking is taken as the value of folding endurance.

6.2. Evaluation of Adhesives Used in TDDS

6.2.1. Adhesive peeling off

This test gives information about the force that is required to remove the adhesive coating from a test substrate, and this is termed as peel adhesion.

6.2.2. Tack property

Thumb tack test. This is one of the qualitative tests, here the force required to remove the thumb adhesive layer of the patch is used as a measure of tack.

Rolling ball tack test. Here in this tack test, a stainless steel ball with a diameter of 7/16 in. is allowed to roll down from an inclined track. The ball comes in contact with the horizontal, upward-facing adhesive.

Quick stick or peel-tack test. The peel force necessary for breaking the bond between an adhesive and substrate is evaluated by pulling the tape away from the substrate at 90 degree angles with the speed of 12 in./min.

Probe tack test. The patch that is to be tested is bought in contact with the tip of the probe, which is required to be clean, thus creating a bond between the probe and the adhesive. The total amount of force necessary to disconnect the probe and the adhesive at a fixed rate is measured as a tack, and it is expressed in grams.

6.3. In Vitro Evaluation

6.3.1. In vitro drug release studies

The paddle over the disc method (USP apparatus V). Dry films of known width are to be incised into definite form, weighed and set flat over a glass plate with an adhesive. The glass plate is further placed in a 500 mL of a dissolution medium or phosphate buffer and equilibrating the apparatus to 37C. The paddle is set at a distance of 2.5 cm from the glass plate and operated at a speed of 50 rpm. Samples are withdrawn at appropriate intervals of time up to 24 h. Samples are analyzed by UV spectrophotometer or HPLC. An experiment performed as triplicate, and the mean value is calculated.

Cylinder modified USP basket (USP apparatus 6). This technique is similar to the USP basket type dissolution apparatus, with the exception that the system is attached to the surface of a hollow cylinder immersed in dissolution medium at 37 ± 5°C.

Reciprocating method (USP apparatus 7). In this method the patches attached to holders have oscillated in small volumes of dissolution medium, thus allowing the apparatus to be useful for systems delivering low concentration of the drug, paddle over-extraction cell method may also be used for the same [22].

6.3.2. Skin permeability studies: Franz diffusion cell

Franz diffusion cell comprises of two chambers. Base (bottom) chamber to hold the buffer or the receiver medium. Upper medium/donor-hold formulation under test. A suitable buffer is selected as dissolution medium. The temperature is maintained at constant throughout the experiment. There will be a sampling port at the receptor compartment. The drug-containing film with a backing membrane was kept in the donor compartment and was separated from the receptor compartment by a skin membrane. The receptor fluid is required to be mixed thoroughly with the aid of magnetic stirring bars. Samples of 3 mL were withdrawn at pre-determined time intervals and were replaced with fresh buffer. Samples were analyzed by UV spectrophotometrically and cumulative percentage drug released was calculated [22, 23].

6.4. In Vivo Evaluation

6.4.1. Animal models

Animals used in these studies include the mouse, rat (hairless), rhesus monkey (hairless), dog (hairless), rabbit, guinea pig, etc. TDDS formulations are applied on a pre-determined bald (shaved) surface of the skin of the animal. Blood samples are collected at different intervals of time to evaluate serum drug concentrations. Critical parameters like C_{max}, T_{max} and elimination half-life were determined.

Skin irritation studies. Healthy rabbits are used for understanding the skin irritation and sensitization by application of TDDS. A healthy rabbit is taken, and its dorsal surface is cleaned, and the hair is shaved from the same area. This surface is then cleaned with the rectified spirit after which the TDDS to be tested applied to the skin. After 24 h, the patch is detached from the skin, and the skin is to be observed for any rashes and classified into five grades depending on the severity of skin damage.