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Original Research Article

Preformulation Assessment of Transdermal Patches of HMG-CoA Reductase Inhibitors with Bioadhesive Polymers as Excipient

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Abstract

The pharmaceutical science and medication distribution has developed tremendously over an era. Many advancements are done in the field of drug distribution technique. Transdermal drug delivery systems (TDDS) have many advantages and represent an excellent alternative to oral delivery and hypodermic injections. Patients apply these patches to their skin, and the active ingredients enter the circulation by simple diffusion, making their way to the tissues where they can exert their therapeutic effects. In this study, thin-layer chromatography, Infra-Red spectroscopy were used to conduct pre-formulation tests on drug and polymer compatibility. Transdermal patch preparation methods are discussed here, various methods are utilized such as casting solution preparation and transdermal patch preparation.

Keywords: Hypodermic injection, diffusion, thin-layer chromatography, pre-formulation.

Introduction

The pharmaceutical sciences, and particularly medication distribution methods, have seen some truly remarkable advancements this century. Recent advancement in the drug transport technique has been widely studied due to the rising realization that traditional methods of drug administration and application can result in excessive toxicity and, in some cases, ineffectiveness. Multi-dose administration of standard drug forms like solid unit dosage form, injection, capsules, and oral liquid dosage form typically results in significant variations in drug content in the blood.

Recent years have seen the development and testing of numerous novel approaches to medication administration. The condition of hypertension respiratory conditions, rhythm disorders, type 2 diabetes, reproductive management, ulcers of the stomach, arthritic osteoarthritis, etc. [1]

The word "TDDS" is commonly used to refer to transdermal drug delivery systems. Patients apply these patches to their skin, and the active ingredients enter the circulation by simple diffusion, making their way to the tissues where they can exert their therapeutic effects. Unlike other methods of pharmaceutical administration, these transdermal patches have a lengthy half-life in the blood of patients. The old techniques of treatment and drug

application have been replaced by this approach because of its efficacy and benefits. It has high patient compliance, can be maintained, and prevents liver damage from medication injections.[2]

Methodology

Preformulation Studies

A drug substance's molecular and physical properties must be determined before it can be formulated into a dosage shape. Medicaments substances definition as well as foundation for medicament's mixture with excipients during dosage form manufacturing are both provided by pre-formulation studies.

In this study, thin-layer chromatography and Infra-Red spectroscopy were used to conduct pre-formulation tests on drug and polymer compatibility.[3]

Thin Layer Chromatography(TLC)

The drug-polymer relationship was investigated using thin layer chromatography. Chromatographic analyses were performed on both the purified drug and the drug combined with the polymers.

The given TLC scheme was utilized-

TLC (Precoated) plates: SD fine chemicals manufactured

Layer Thickness: 200µm Separation

Adsorbant Layer: Silica gel G was used

Procedure: Rising Tech.(Ascending) was employed

Dimensions: TLC plate 10x20 centimeter

Benzene	Chloroform	Methanol	Acetic acid
3	6	1	0.1

Mobile phase

Sample's Preparation: For spotting, the samples and an appropriate quantity of purified substance had been dissolved within chloroform: methanol (1:1).

Volume utilized:10 µL

Recognition: UV cabinet chamber.[4]

Spectroscopic analysis with the FTIR

The JASCO-410 FTIR spectrophotometer utilized to test the medicament's and polymer's compatibility. Transparent, thin pellets were made by completely combining 1 part of the material with three portions of dried potassium bromide. After this, the pellets were examined in the infrared area, and the resulting spectra were documented and reviewed. [5,12]

Atorvastatin Standard Graph Preparation:

Standard Stock Solution

Methanol was used to create a stock solution of atorvastatin calcium (1mg/ml).

Atorvastatin Calcium Scan

Absorption peaks at 241 nm was determined by scanning the above-mentioned standard stock solution in the UV region (200-400 nm); this frequency was then used for further investigation.

Standard Plot

A number of dilutions were made with standard stock sol. utilizing phosphate buffer pH 7.4 The linear range for Atorvastatin calcium was found to be between 4 and 22 mcg/ml. After diluting with a phosphate solution at pH 7.4, the final concentrations were 4, 8, 12, 16, and 20 mcg/ml. At 241 nm, a SHIMADZU Ultraviolet 1700 spectrophotometer was used to compare the absorbances to a reagent blank. Absorbances at 241

nanometers were employed to calibrate the medicament's concentrations. [6,7]

Preparations Of Transdermal Patch [8,9,10,11]

Transdermal Patch Preparation Methods In General:

Here, Atorvastatin calcium transdermal patches of the matrix variety were made using molding methods. For this purpose, a flattened circular glass mold with a diameter of 4.5centimeter, height 1centimeter, and 5.91 cm^2 was the entire surface area that was created.

A) Casting Solution Preparation:

Polymers were dissolved in a combination of the methanol as well as chloroform at a 1:1 ratio to create the casting solutions. The different polymer solutions were then combined to form a uniform solution, and the medication, plasticizer, and permeation boosters were added separately. To release the trapped air, it was set away and left undisturbed.

B) Transdermal Patch Preparation:

On the surface of mercury, about 3ml of casting solutions have been pipetted onto circular glass cases made for the purpose. Dried the glass molds holding the casting solutions at a ambient temperature for whole day and dried prepared patches into an oven at 40 degrees Celsius to 45 degrees Celsius for half an hour helps get rid of any lingering solvents.

The pieces were sliced off into 4.4cm diameter circular plates (entire SA=15.21cm^2). For future research, aforementioned patches had been individually covered within foil then placed within a desiccator.

Result and Discussion

Using polymers such as, EC, ERS100, glycerine as well as HPMC as a plasticizer in addition with Dimethyl sulfoxide as a penetration enhancer, a transdermal drug delivery method for atorvastatin calcium was created. Twenty-one patches were tested for their tensile strength, hardness, drug content, moisture uptake, tensile strength, and overall physical look. Stability studies were performed on the most promising formulations after in vitro studies of drug release across a cellulose barrier had been completed.

Studies of Compatibility

Studies on the drug's compatibility with plastics found no evidence of a chemical reaction between the two. Physicochemical characteristics were assessed.

Thin layer chromatography

TLC was conducted on both the pure drug as well as the drug together employing polymers(fig:1), as well as Rf values are listed below in table no.1. There is no drug-polymer chemical reaction, as shown by the high Rf readings.

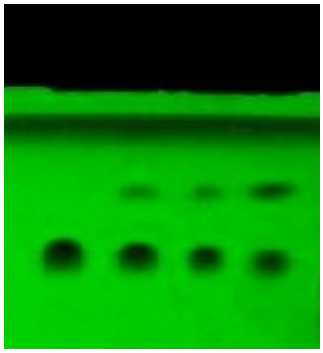

Fig. 1: TLC-Thin layer chromatogram

Table 1: Rf values

S. No	Sample	Rf value
1	Drug	0.48
2	Drug+HPMC+EC	0.47
3	Drug+HPMC+ERS100	0.47

FT-IR spectroscopic analyses

Spectra from a JASCO FT/ IR spectrophotometer were used to determine whether or not the drug was compatible with the polymers (figures 2 to 8). Polymer–drug mixture spectra were found to be consistent with those of the purified drug. There was no change in the shape of any peaks, indicating that there was no molecular reaction among the drug as well as the polymer.

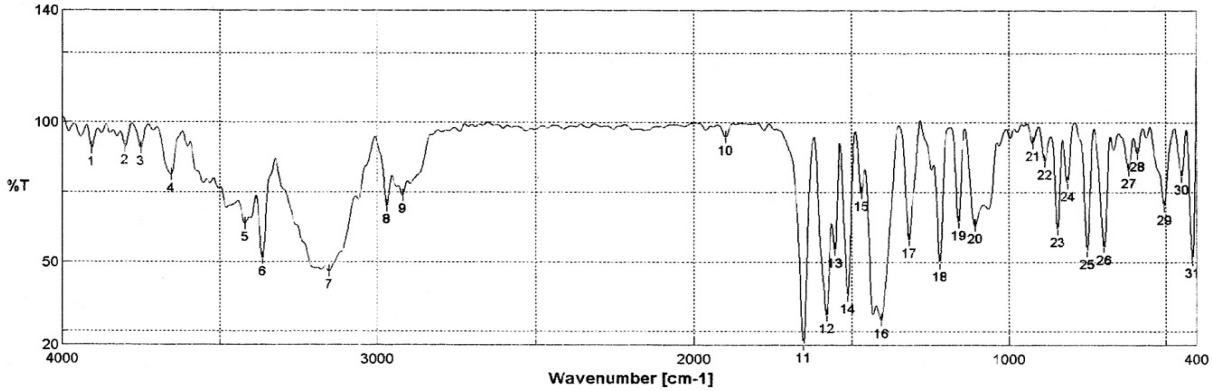

Fig. 2: Atorvastatin calcium IR Spectrum

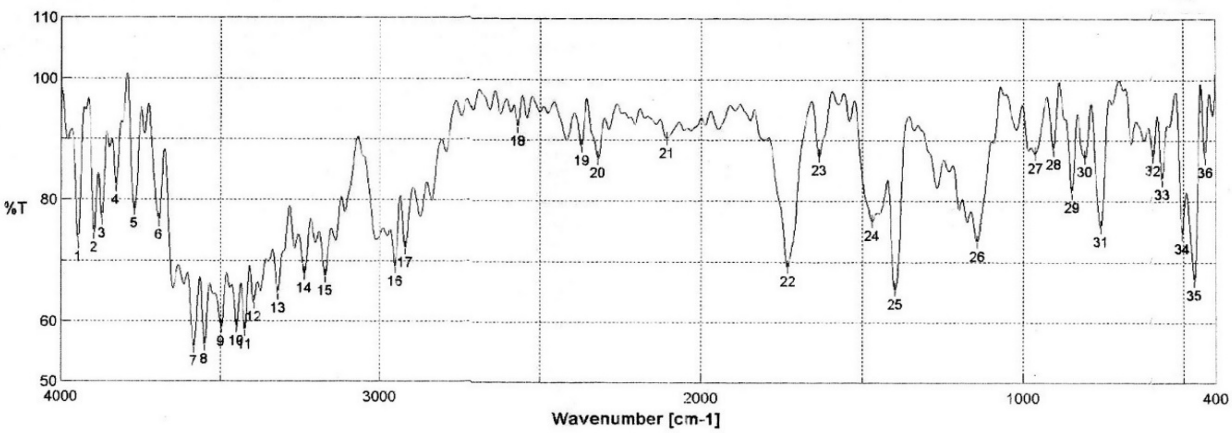

Fig. 3: ERS100 IR Spectrum

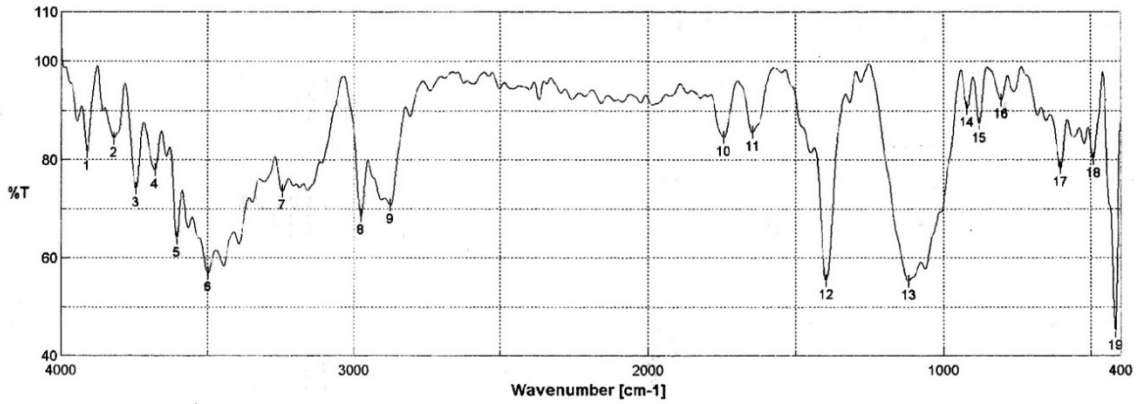

Fig. 4: EC IR Spectrum

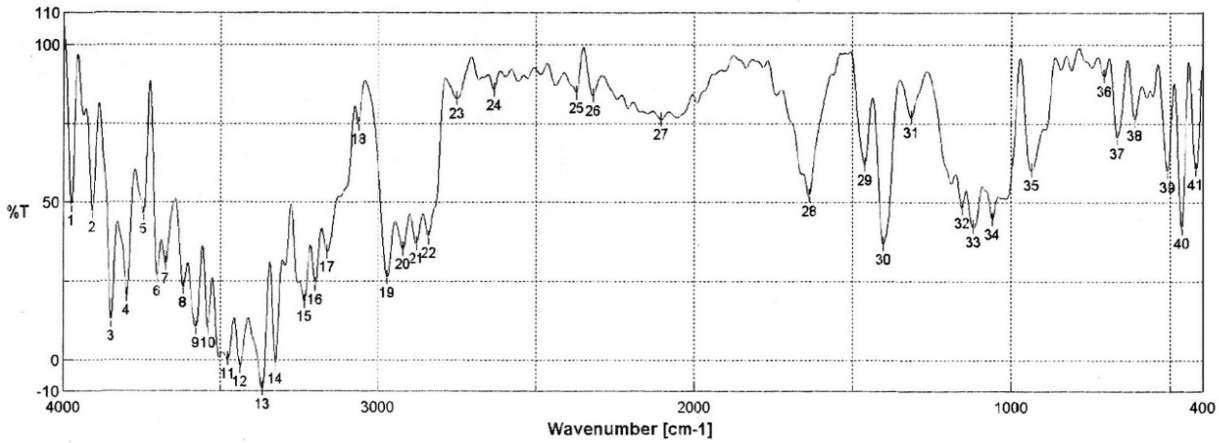

Fig. 5: HPMC IR Spectrum

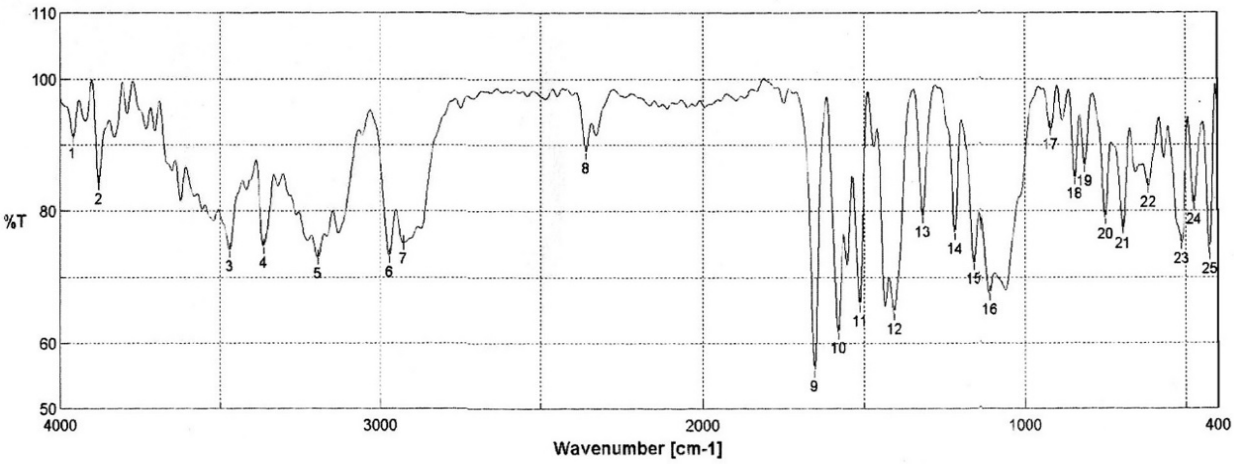

Fig. 6: HPMC+EC+Drug IR Spectrum

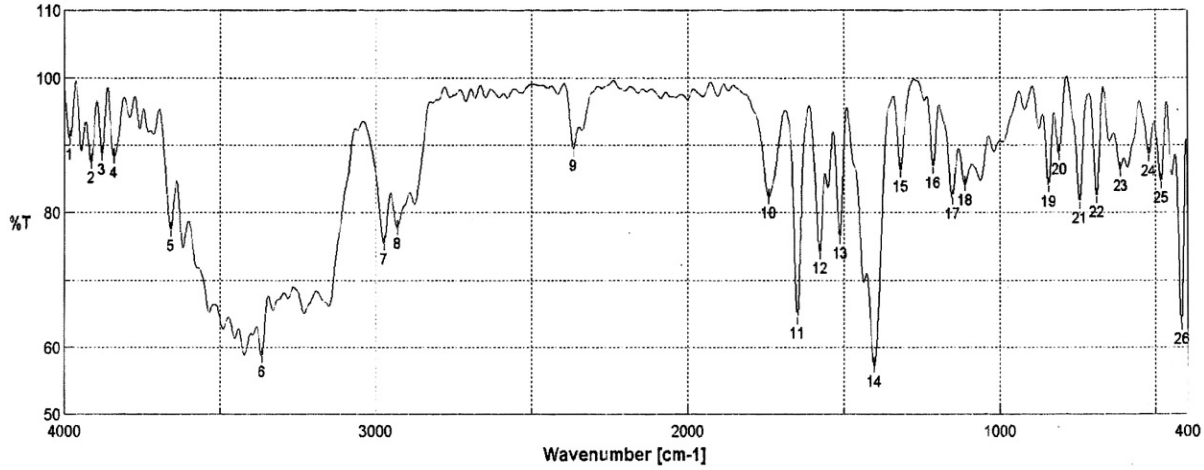

Fig. 7: EC+ERS100+Drug IR spectrum

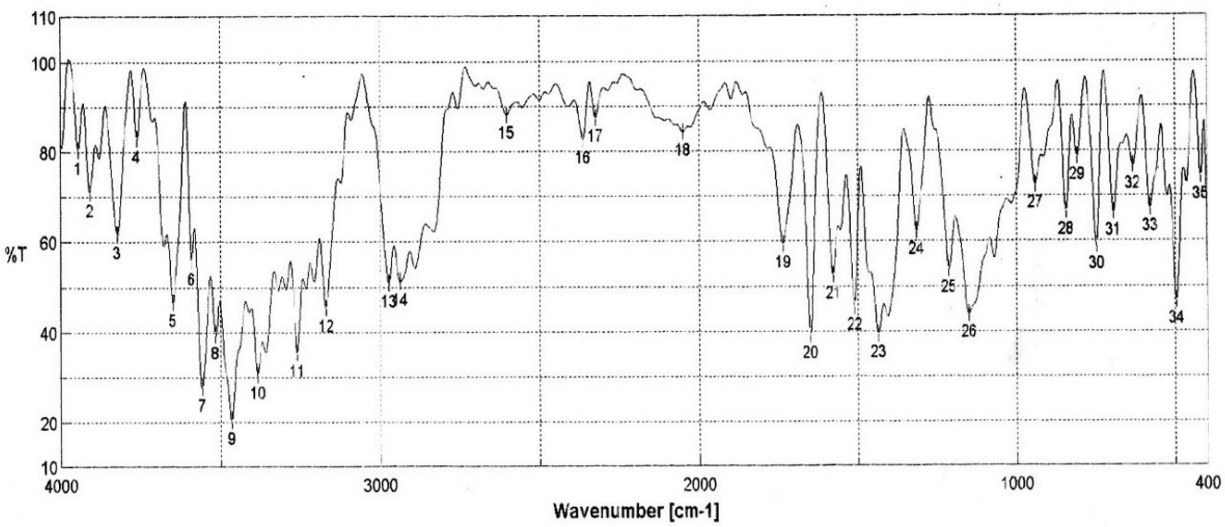

Fig. 8: HPMC+ERS100+Drug IR Spectrum

Conclusion

The preformulation evaluation of the transdermal patches of 3 hydroxy -3 methyl glutaryl coenzyme a (hmg-coa) reductase inhibitors using bio adhesive polymers as excipients was done. In the present research thin-layer chromatography, Infra-Red spectroscopy were used to conduct on drug and polymer compatibility with the drug was also checked and the results was within limit. There was no sign of incompatibility. Casting solution preparation and transdermal patch preparation was employed for the preparation of transdermal patches. Its was concluded that the polymer was compatible with the drug and these can be utilized for the preparation of the transdermal patches.

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