

Development of a sustainable transdermal drug delivery system for the treatment of dermatological conditions utilizing porous and modified rubber materials

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Abstract

Natural rubber (NR) is widely used bio polymer and can be easily modified due to its unsaturation. Various transdermal drug delivery systems have been developed utilizing NR latex. In all these instances drugs were incorporated through physical methods which do not demonstrate significant capability for controlled drug release. However, in this study uncontrolled drug release of physically incorporated rubber was achieved by chemical bonding between 3-acetyl coumarin ( used as a model drug) and amine modified rubber. Later, a porous rubber sheet was prepared using the Dunlop process. The 3-acetyl coumarin was then physically incorporated into the porous rubber sheet. The drug release from both sheets was evaluated using an artificial sweat solution prepared according to the EN 1811 standard. Results indicate that the chemically bonded rubber sheet exhibits superior control over drug release compared to the physically incorporated porous rubber sheet.

Introduction

- Transdermal drug delivery systems (TDDS) are topically administrated medications, contacted to the surface of skin and deliver a specific dose of drugs across a skin barrier in to the systematic blood stream.
- NR has attracted significant attention in transdermal drug delivery systems due to its cost-effectiveness, eco-friendly nature, bioavailability, and properties such as elasticity, flexibility, and easy film formation.
- In this study, 3-acetyl coumarin was used as a transdermal model drug which have properties such as anti cancer, anti diabetic, Anti-coagulant and anti bacterial activities.
- The synthesized 3-acetyl coumarin was incorporated into an amine modified natural rubber latex and drug releasing efficiency was were evaluated. Furthermore, 3-acetyl coumarin was physically incorporated into a porous rubber sheet and drug releasing was studied in order to compare the drug releasing efficiency.

Conclusion

- The drug release rate from the chemically bonded rubber sheet ( $0.2142\text{ mol}\cdot\text{g}^{-1}\cdot\text{min}^{-1}$ ) was significantly lower than that from the physically bonded porous rubber sheet ( $4.0094\text{ mol}\cdot\text{g}^{-1}\cdot\text{min}^{-1}$ ) before reaching a plateau. This indicates that the chemically bonded sheet offers superior control over drug release, likely due to the presence of a labile imine bond between the modified rubber sheet and the drug.

Methodology

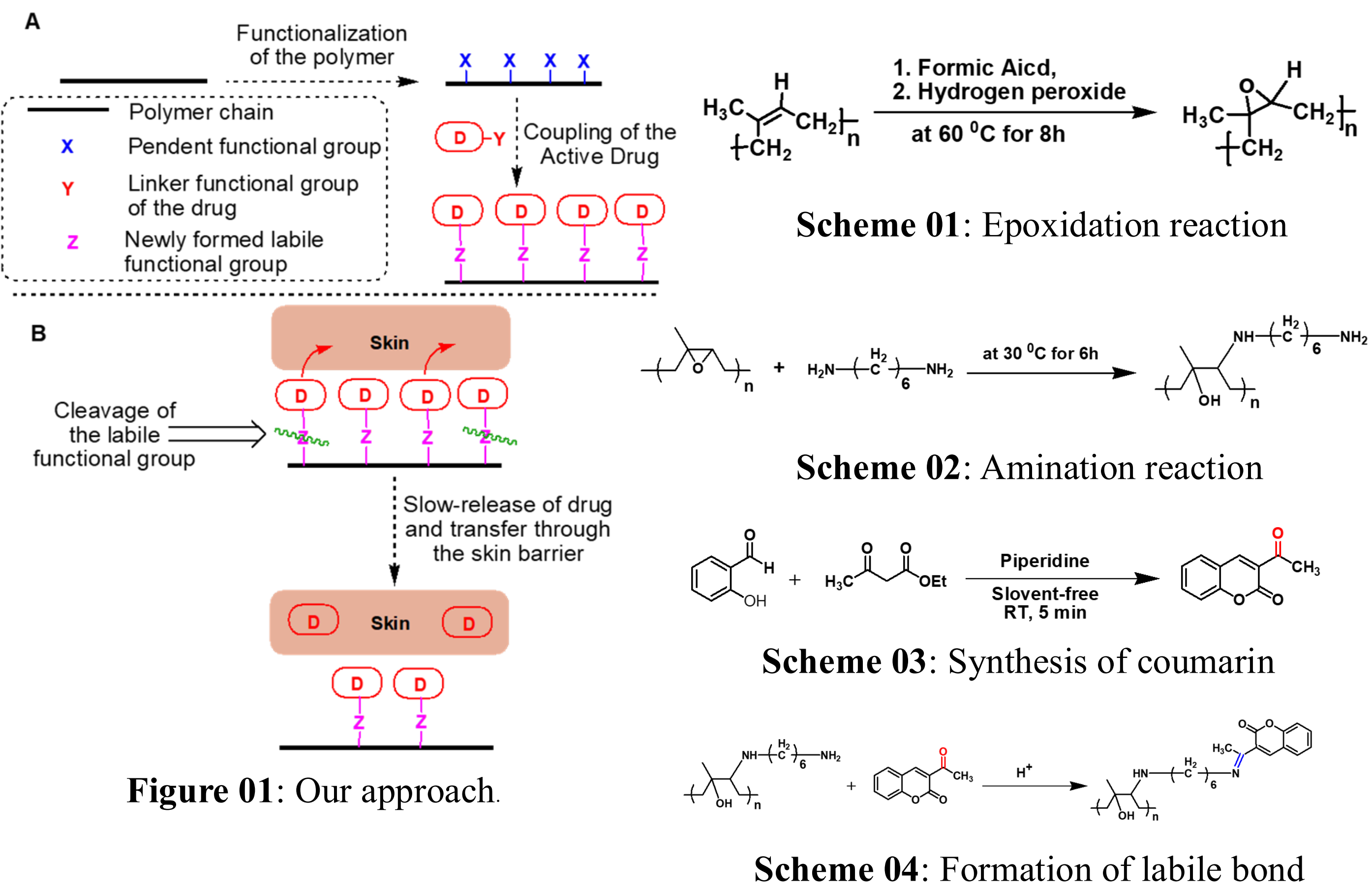
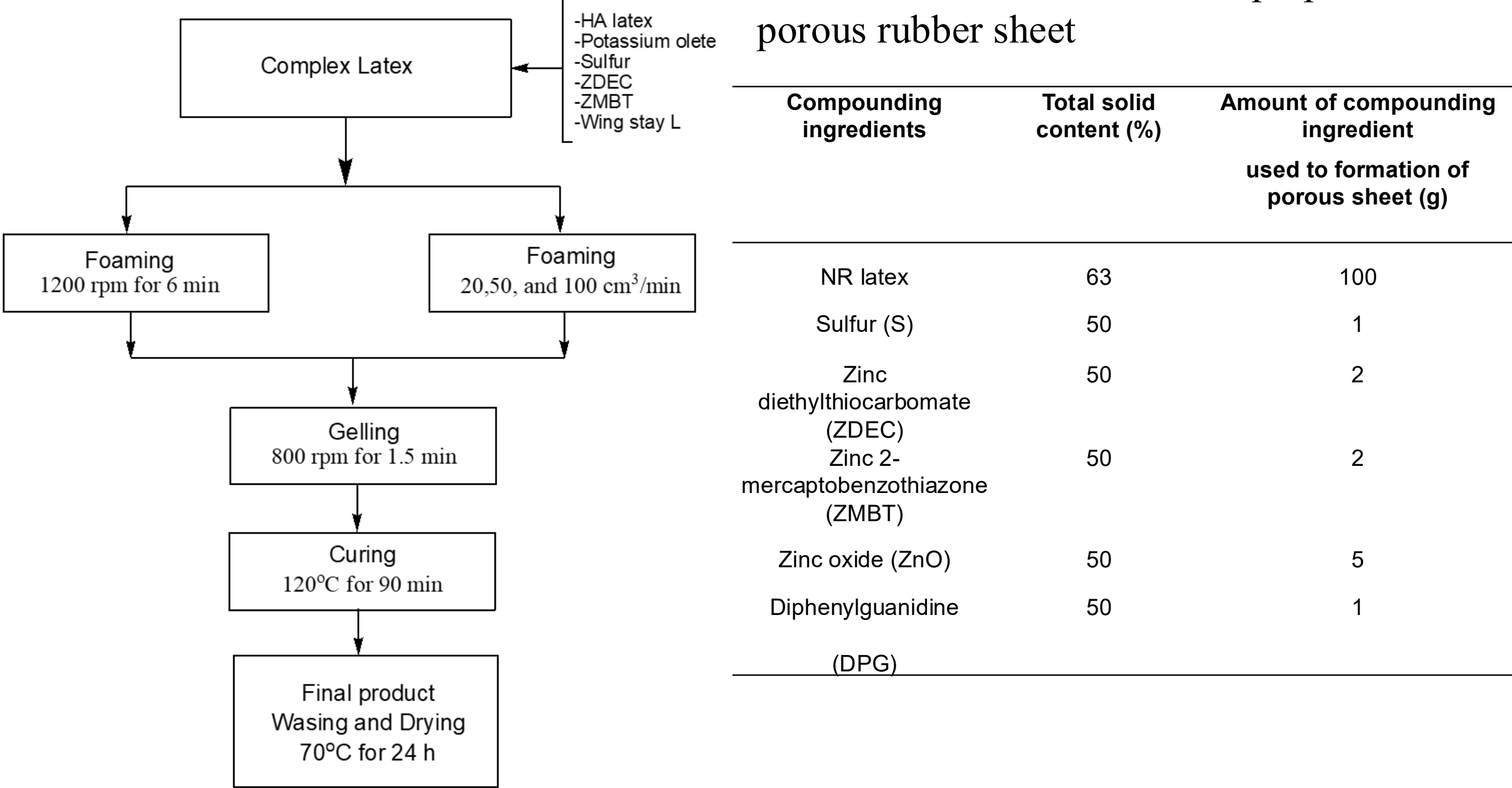


Figure 01: Our approach.



Results and discussion

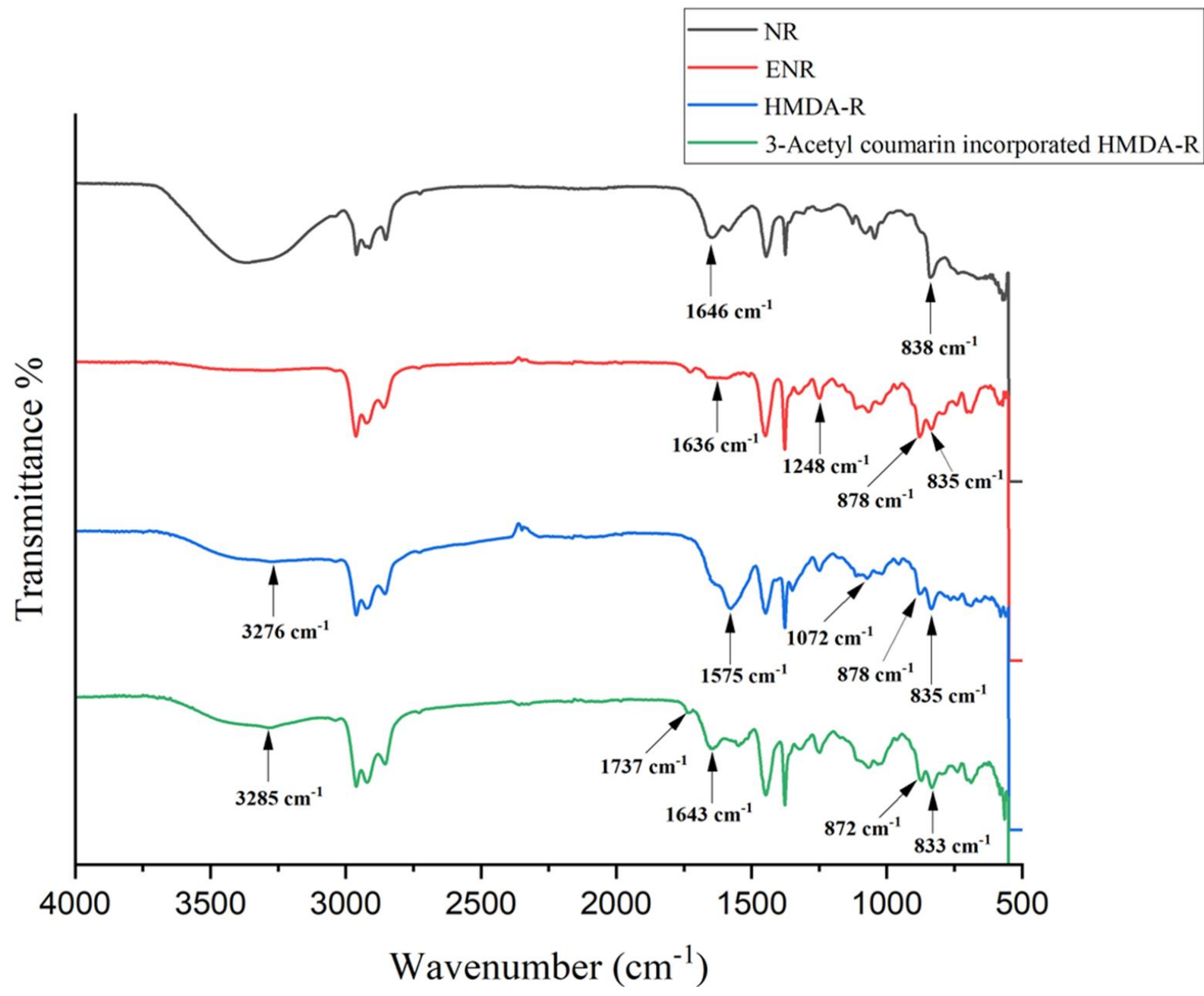


Figure 03: FTIR spectra of NR, ENR, HMDA-R, 3-acetyl coumarin incorporated HMDA-R.

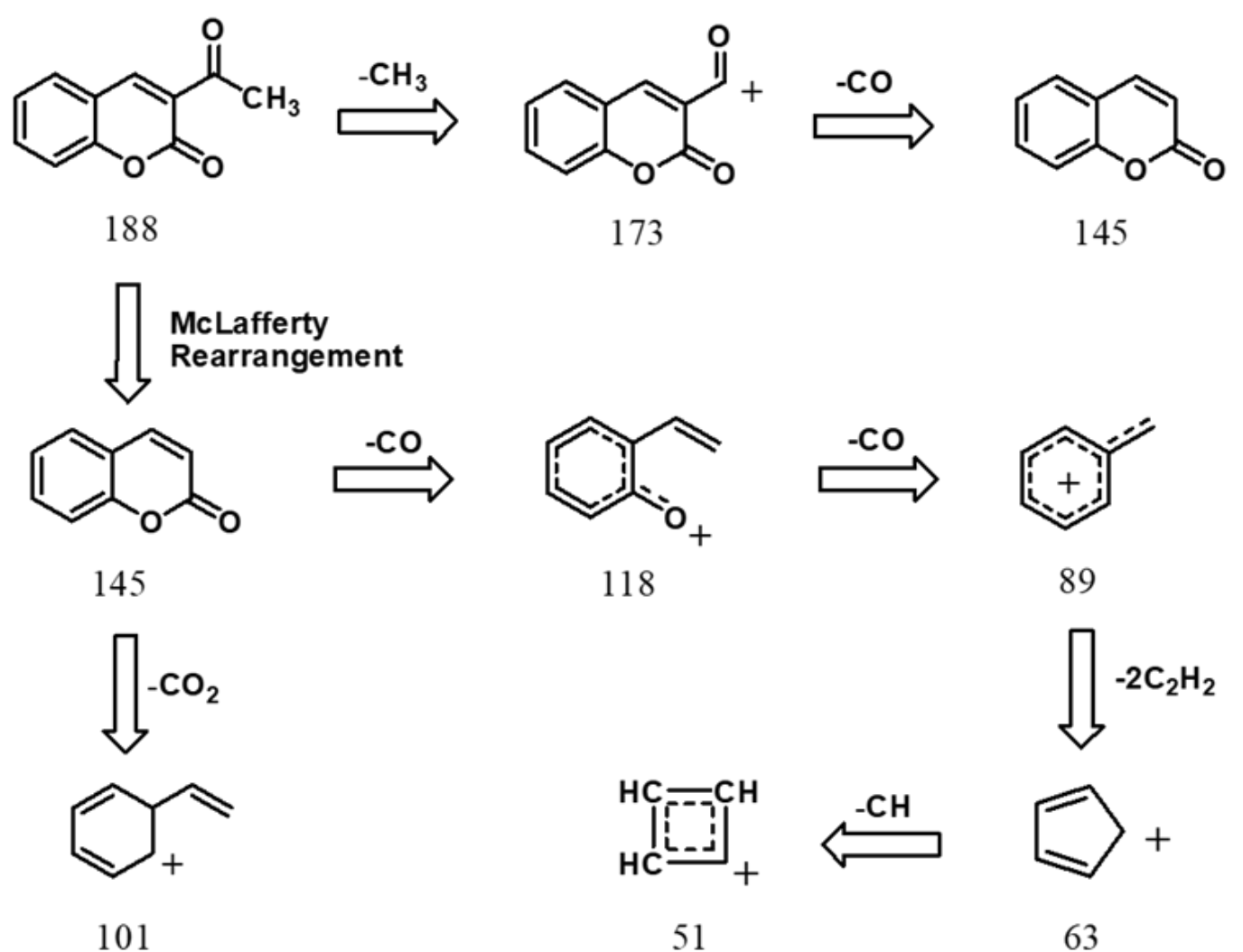


Figure 05: Mass spectrum analysis of 3-acetyl coumarin with possible fragments.

- The above peaks of the mass spectrum confirmed the formation of 3-acetyl coumarin .

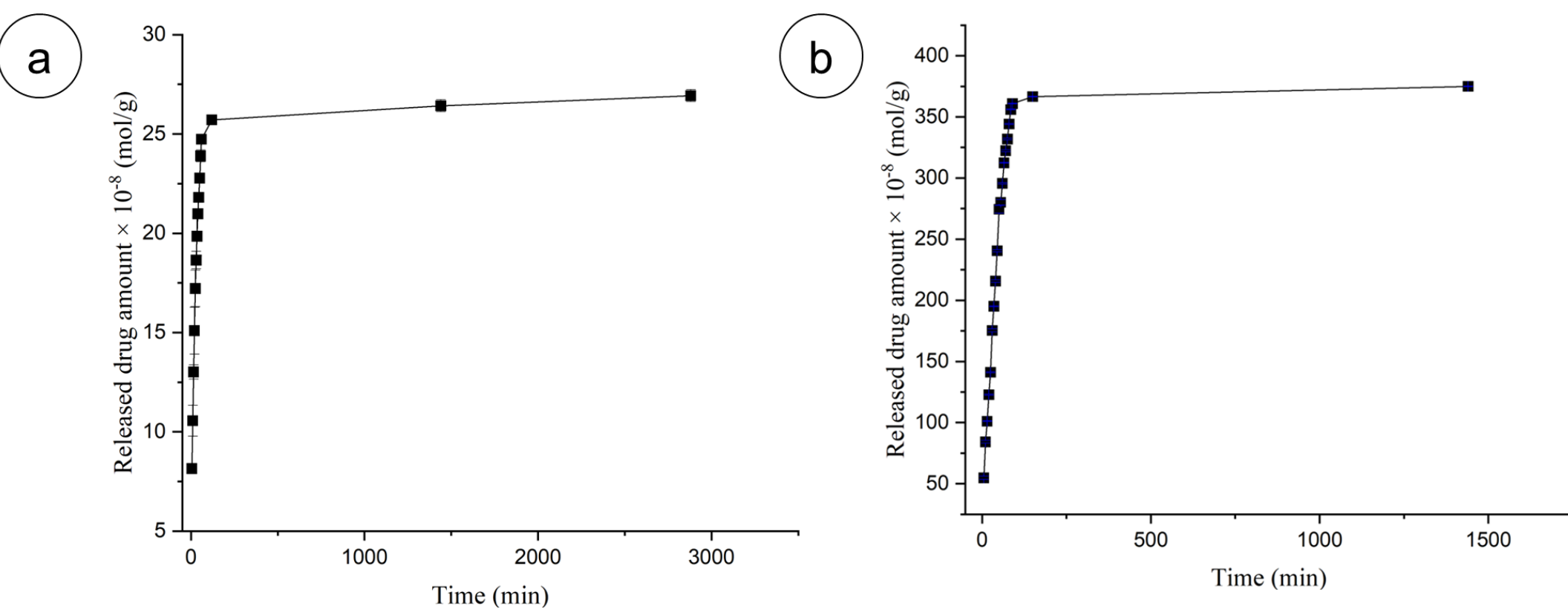


Figure 05: Cumulative drug release curves of (a) drug chemically bonded rubber sheet (b) drug physically incorporated rubber sheet.

**Table 02: FTIR spectrum data**

| Type of bond vibration      | Characteristic peaks (cm <sup>-1</sup> ) (Figure 7) | Characteristic peaks according to References (cm <sup>-1</sup> ) |
|-----------------------------|-----------------------------------------------------|------------------------------------------------------------------|
| N-H stretching              | 3285                                                | 3200-3500                                                        |
| C-O-C symmetric stretching  | 833                                                 | 831-841                                                          |
| C-O-C asymmetric stretching | 872                                                 | 870-880                                                          |
| N-H bending                 | 1547                                                | 1580                                                             |
| C-N Stretching              | 1068                                                | 100-1200                                                         |
| C=N stretching              | 1643                                                | 1620-1690                                                        |
| C=O ring Stretching         | 1737                                                | 1700-1750                                                        |

- The above peaks of the FTIR spectrum confirmed the modifications of NR and drug incorporation.

Figure 04: TGA curves for NR,ENR,HMDA-R, 3-acetyl coumarin incorporated HMDA-R.

- The TGA curves confirmed the modifications of NR and drug incorporation and thermal stability after each modification.

**Table 03: GC-MS Chromatogram data**

| Compound No. | Retention time (min) | Relative intensity (%) | Total intensity (%) |
|--------------|----------------------|------------------------|---------------------|
| 1            | 20.825               | 100                    | 87.131              |
| 2            | 44.319               | 7.29                   | 6.353               |
| 3            | 50.856               | 7.48                   | 6.516               |

- The curves in figure 11 confirmed controlled drug release of drug chemically bonded rubber sheet compared to drug physically incorporated porous rubber sheet.

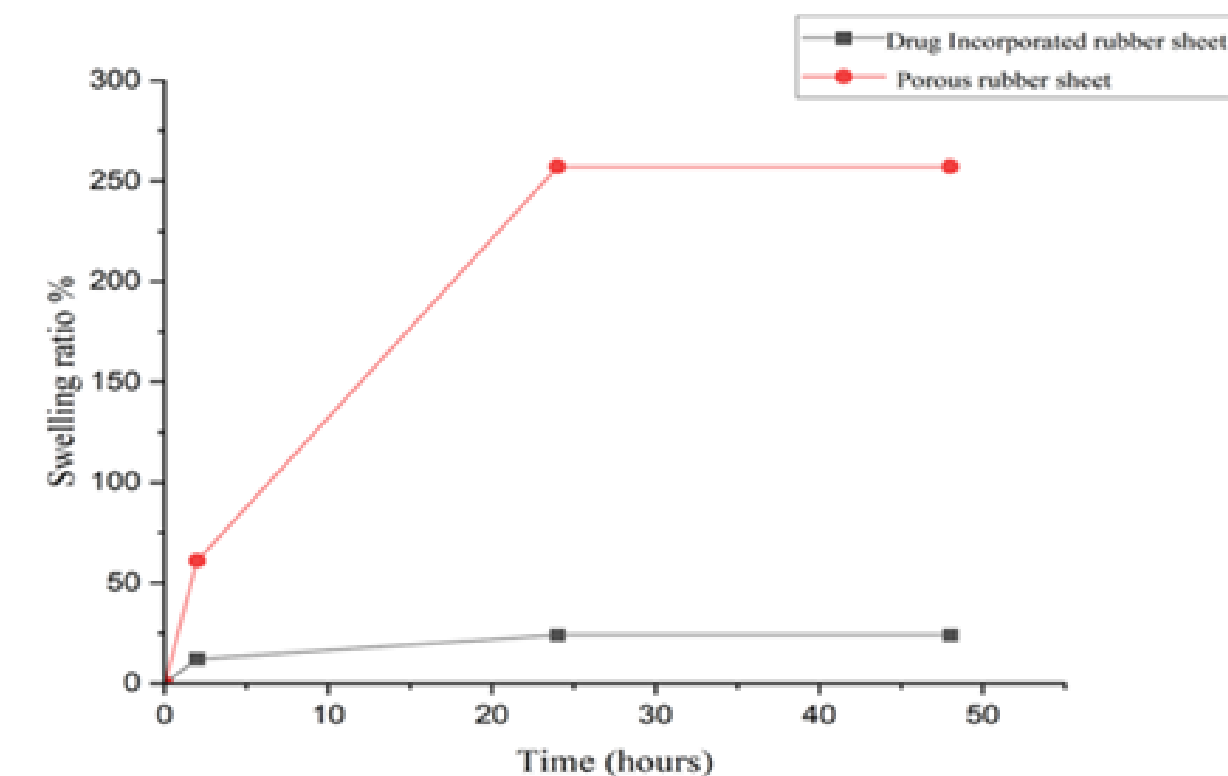


Figure 06: Curves of swelling ratios of Rubber sheet (chemically drug bonded) and porous rubber sheet.