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RESEARCH PAPER

Characterization and Evaluation of Tenoxicam Coprecipitates

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ABSTRACT

Tenoxicam is a nonsteroidal anti-inflammatory drug belonging to the oxicam group. The drug is slightly soluble in water. In a trial to increase its dissolution, different commonly used excipients were selected to prepare coprecipitates with tenoxicam. The coprecipitates were prepared using the solvent evaporation method, and the ratio used was 1:3 drug to additive. The prepared coprecipitates were subjected to a dissolution study, and they were characterized using infrared (IR) and differential scanning calorimetry (DSC) techniques. Dissolution profiles of most of the prepared coprecipitates demonstrated higher dissolution than pure tenoxicam. The characteristic peaks of tenoxicam in the IR spectrum disappeared in the spectra of all the prepared coprecipitates except those prepared with sodium chloride, for which the IR spectrum was identical to that of the pure drug. The characteristic peaks of tenoxicam disappeared in the DSC thermograms of the coprecipitates under study, indicating a change in structure from pure tenoxicam. Characterization of the coprecipitates by IR and DSC techniques revealed structural changes in the prepared coprecipitates from the plain drug, which may account for increased dissolution rates.

Key Words: *Coprecipitates; Dissolution; Tenoxicam.*

INTRODUCTION

Tenoxicam is 4-hydroxy-2-methyl-*N*-(2-pyridyl)-2-H thieno [2,3e][1,2] thiazine-3-carboxamide-1,1-dioxide(1). It has anti-inflammatory, analgesic, and antipyretic properties, and it also inhibits platelet aggregation (2). In vitro tests of leukocyte peroxidase suggest that tenoxicam may act as a scavenger for active oxygen at the site of inflammation. These pharmacological effects explain, at least in part, the successful use of tenoxicam in the treatment of painful inflammatory and degenerative disorders of the musculoskeletal system (3).

The formation of solid dispersions is an effective method for increasing the dissolution rate of poorly soluble drugs, hence improving their bioavailability (4). Hydrosoluble polymers such as polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) were used to improve the dissolution properties of naproxen (5).

Iwata and Ueda (6) studied the dissolution of glibenclamide with PVP. The prepared coprecipitates exhibited higher dissolution rates compared to intact glibenclamide, and formation of coprecipitates was confirmed by differential scanning calorimetry (DSC) and infrared (IR) spectroscopy.

Tenoxicam is very slightly soluble in water (0.01 g/100 ml), so in a trial to increase its dissolution, different water-soluble carriers were incorporated with the drug. The dissolution data for the prepared coprecipitates were interpreted through IR and DSC studies.

EXPERIMENTAL

Materials

Materials used were tenoxicam (Chemo Iberica), anhydrous lactose (BP), sorbitol, sodium benzoate, PEG4000, PVP K90, sodium chloride (Sigma Chemical Co., St. Louis, MO). All other materials and solvents were analytical reagent grade.

Methods

Preparation of Tenoxicam Coprecipitates

Coprecipitates of tenoxicam with different excipients were prepared in the ratio of 1:3 drug to carrier. The additives used were lactose, sorbitol, sodium chloride, sodium benzoate, PEG4000, and PVP K90. The coprecipitates were prepared using the solvent evaporation method. The calculated amounts of tenoxicam and each of the aforementioned additives were dispersed homogeneously in the least amount of dichloromethane, and then the solvent was evaporated. The obtained coprecipitate was kept over anhydrous calcium chloride in a dessicator. The dried mass was pulverized and sieved, and the fraction of the power that passed through a 160-μm sieve and were retained on a 100-μm sieve was collected and used for further investigations.

Dissolution of Tenoxicam Coprecipitates

An accurately weighed amount of the powdered coprecipitate containing 20-mg tenoxicam was subjected to a dissolution study using the USP type I dissolution tester. The dissolution medium was 400 ml Sorensen phosphate buffer (pH 7.4) maintained at 37°C, and the stirring rate was 50 rpm. Samples were withdrawn at different time intervals and analyzed for tenoxicam content spectrophotometrically at λ 368 nm. the dissolution study was performed for plain drug for comparison.

Infrared Study of Tenoxicam Coprecipitates

A fresh sample of the coprecipitate (2–3 mg) was mixed with approximately 400 mg of dry potassium bromide powder. Mixing was done in a dry mortar, and the mixture was compressed into a disk under a pressure of 1000 to 1500 pounds per square inch. The IR spectra of the drug and the freshly prepared coprecipitates were determined.

Differential Scanning Calorimetry of Tenoxicam Coprecipitates

The DSC of tenoxicam and its coprecipitates was performed using a Shimadzu DSC-50 thermal analyzer (Kyoto, Japan). Samples were placed in an aluminum pan and heated at a rate of 10°C/min with indium in the reference pan.

RESULTS AND DISCUSSION

Dissolution Studies

The results of the dissolution study of tenoxicam coprecipitates are illustrated in Figs. 1 and 2.Tenoxicam is slightly soluble in water, and this is reflected in the extent of drug dissolved after 1 hr, which was 67.9%. The incorporation of tenoxicam in different water-soluble carriers resulted in an increase in the drug dissolved to variable extents. The amount of tenoxicam dissolved after 1 hr was found to be 94.7%, 82.8%, 78.0%, 76.9%, 69.5%,

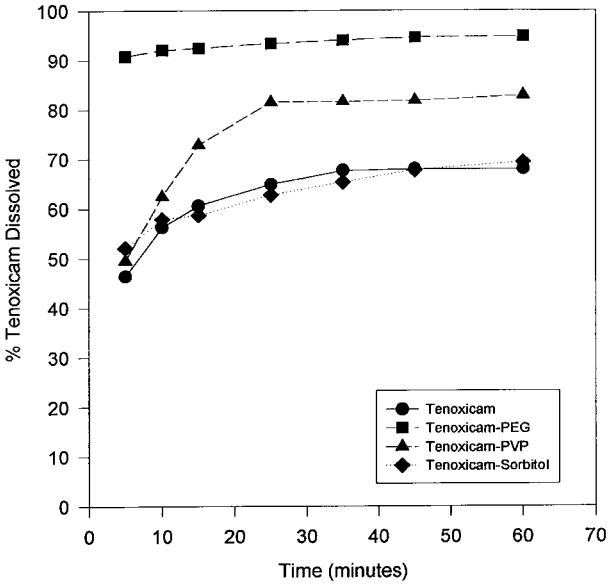

Figure 1. Dissolution of tenoxicam from coprecipitates with PEG, PVP, and sorbitol.

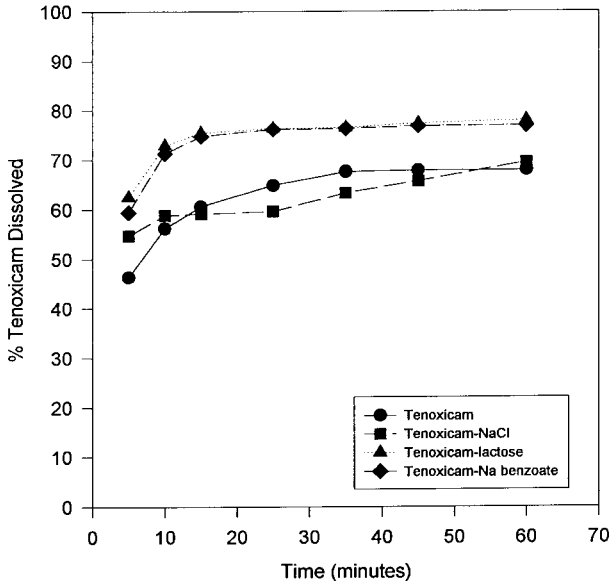

Figure 2. Dissolution of tenoxicam from coprecipitates with sodium chloride, lactose, and sodium benzoate.

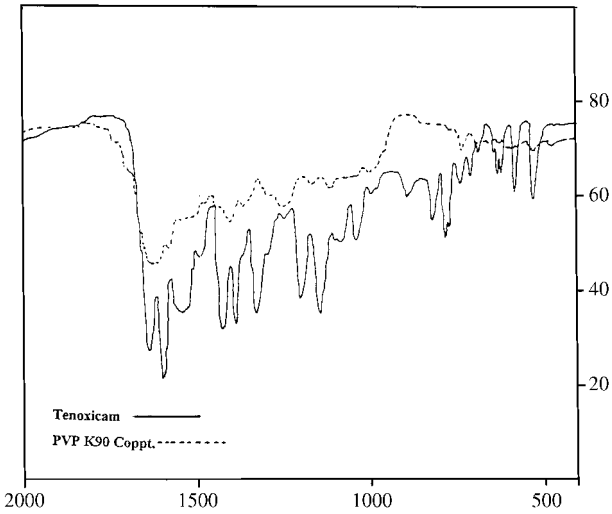

Figure 4. Infrared spectra of tenoxicam and tenoxicam–polyvinylpyrrolidone coprecipitate.

and 69.3% for PEG4000, PVP K90, lactose, sorbitol, sodium chloride, and sodium benzoate, respectively.

The increase in the dissolution of the coprecipitates prepared using PEG4000 and PVP K90 could be attributed to the fact that these water-soluble polymers intimately encircle the hydrophobic drug particles of tenoxicam, thus decreasing their aggregation and increasing their wettability, resulting in an enhancement in drug dissolution (7). The drug molecules, when prepared in a solid dispersion with those water-soluble polymers, crystallize in very minute crystals embedded in polymeric matrices (8). This results in rapid dissolution of the embedded drug.

The tenoxicam-lactose coprecipitates showed an increase in dissolution compared to plain drug. Such an effect could be attributed to the fact of the water solubility and hydrophilicity of lactose, which results in a change in the hydrophobic powder bed of tenoxicam and

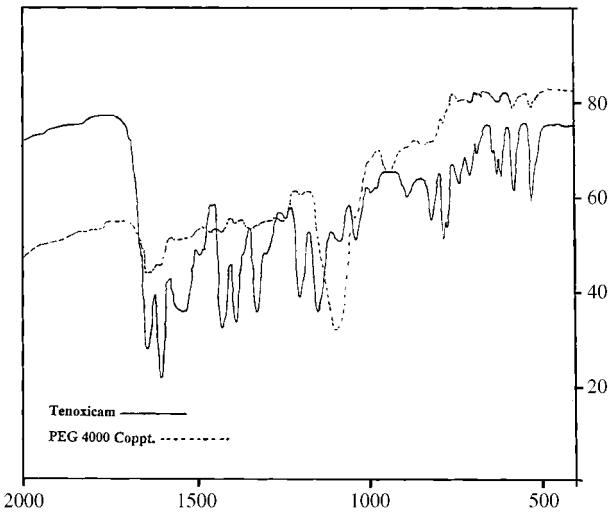

Figure 3. Infrared spectra of tenoxicam and tenoxicam–polyethylene glycol coprecipitate.

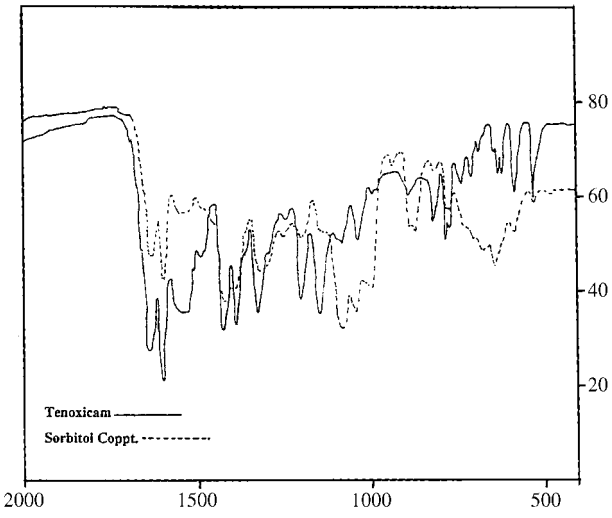

Figure 5. Infrared spectra of tenoxicam and tenoxicam-sorbitol coprecipitate.

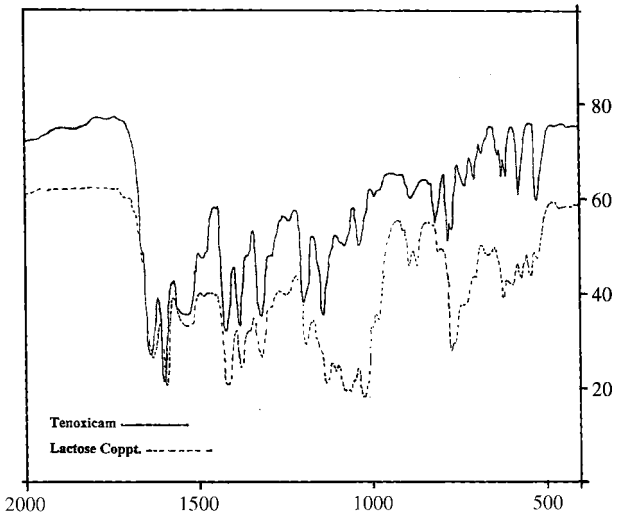

Figure 6. Infrared spectra of tenoxicam and tenoxicam-lactose coprecipitate.

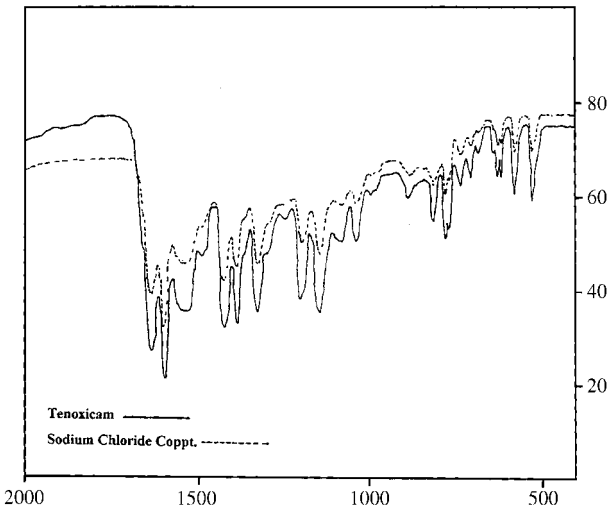

Figure 8. Infrared spectra of tenoxicam and tenoxicam–sodium chloride coprecipitate.

its change to a more hydrophilic one, resulting in an increase in the extent of dissolution (9).

The effect of sodium benzoate as a hydrotropic salt commonly used to increase the dissolution was not evident in this study. Such a masked effect could be due to the low concentration of sodium benzoate used. Usually, the hydrotropic salts are used in higher ratios (10) to exert their desired effect of increasing dissolution than the ratio used in this study; here, the 1:3 drug-to-polymer ratio was not sufficient to increase the wettability and dissolution of the hydrophobic tenoxicam.

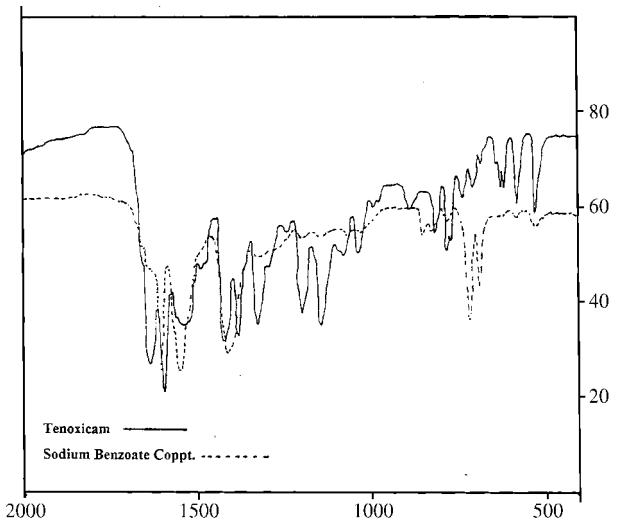

Figure 7. Infrared spectra of tenoxicam and tenoxicam–sodium benzoate coprecipitate.

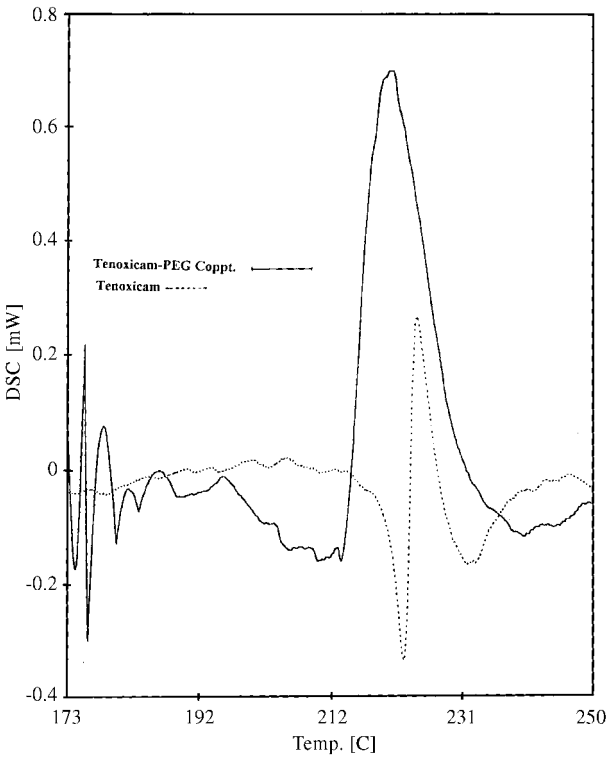

Figure 9. DSC thermogram of tenoxicam and its polyethylene glycol coprecipitate.

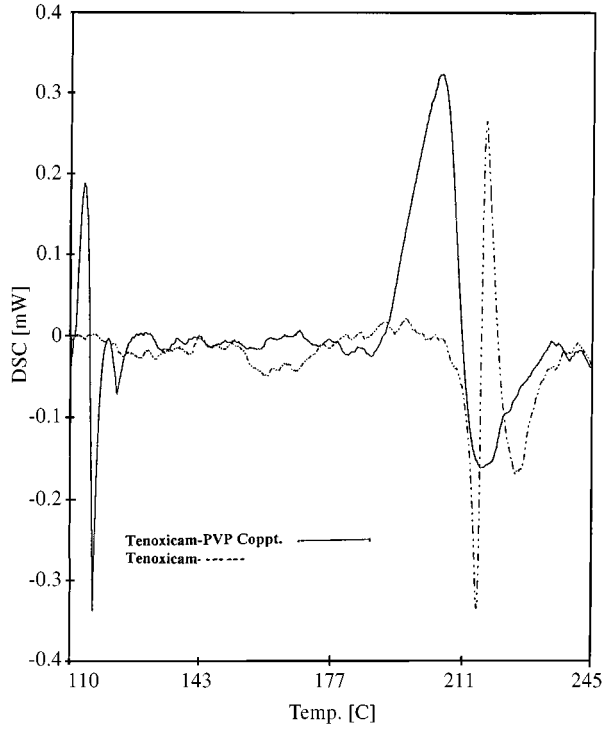

Figure 10. DSC thermogram of tenoxicam and its polyvinylpyrrolidone coprecipitate.

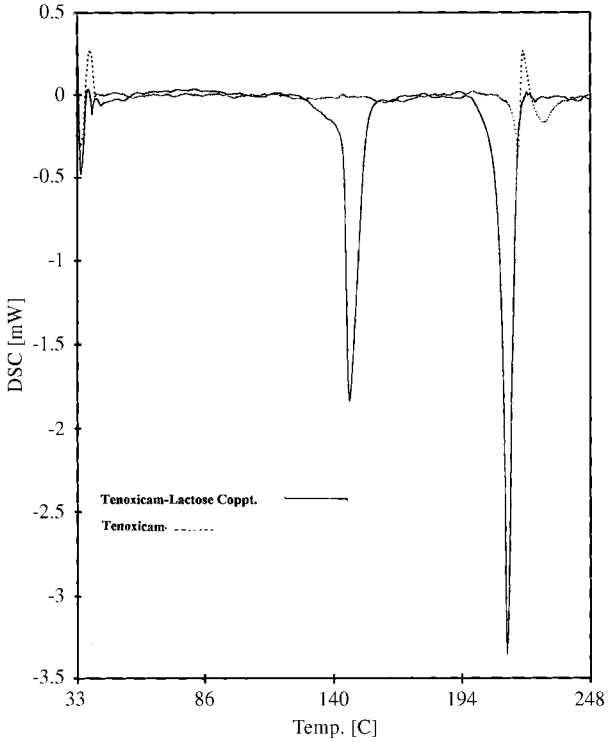

Figure 12. DSC Thermogram of tenoxicam and its lactose coprecipitate.

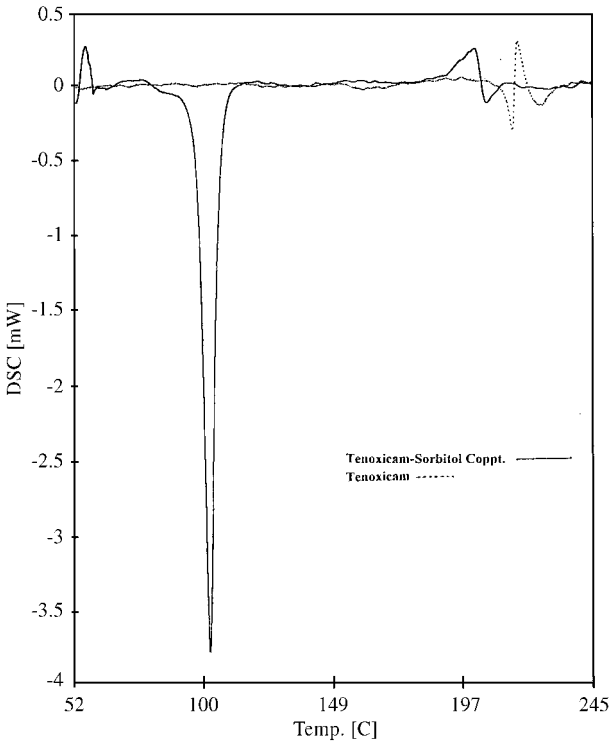

Figure 11. DSC thermogram of tenoxicam and its sorbitol coprecipitate.

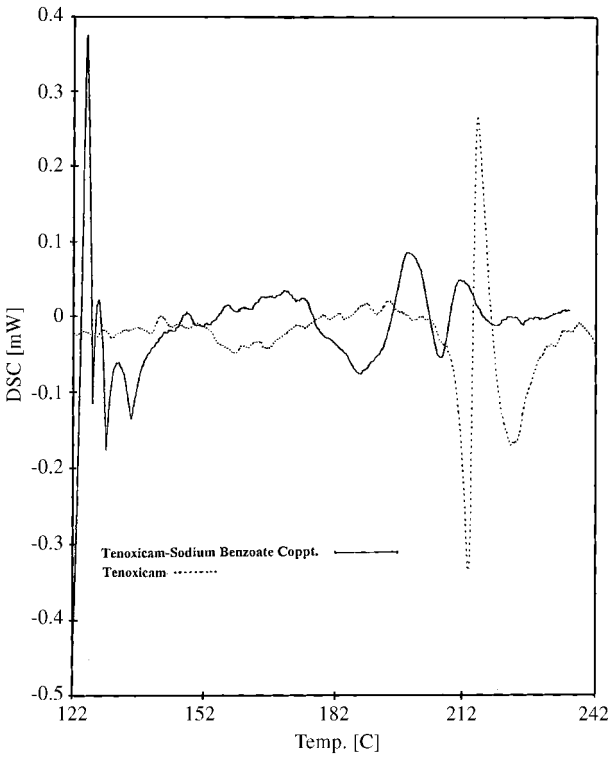

Figure 13. DSC thermogram of tenoxicam and its sodium benzoate coprecipitate.

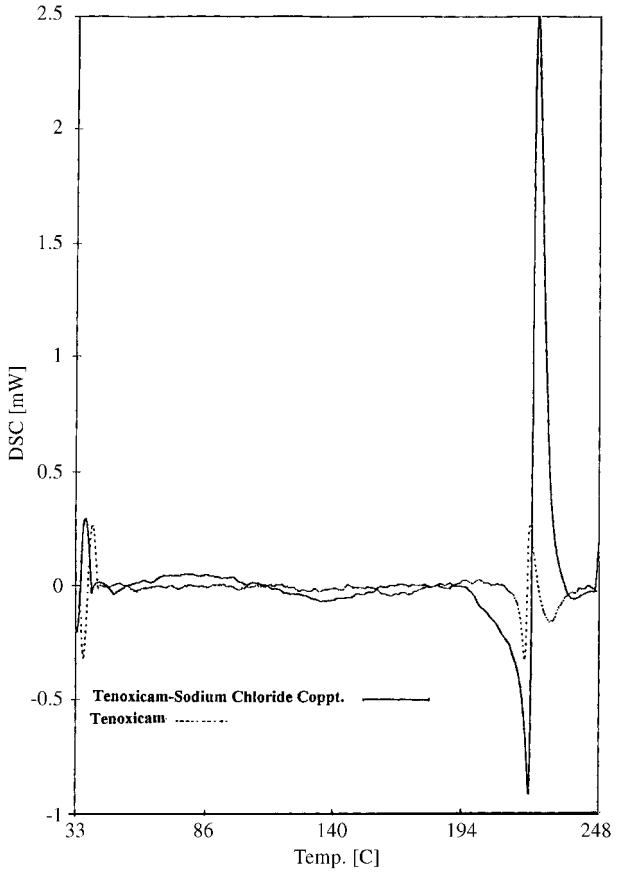

Figure 14. DSC thermogram of tenoxicam and its sodium chloride coprecipitate.

Infrared Studies

The infrared spectra of tenoxicam coprecipitates were compared with that of plain drug with the aim of obtaining more information about the possible changes in the prepared coprecipitates. The IR spectra are presented in Figs. 3–8. The characteristic peaks of tenoxicam in the IR spectrum are located at 1640, 1600, 1500, and 1420.

These characteristic peaks disappeared from the spectra of all the prepared coprecipitates except those prepared with sodium chloride, for which the IR spectrum was identical to that of the pure drug. These spectral changes of the prepared coprecipitates could account for their increased dissolution, indicating structural changes in the coprecipitates from the parent drug, whereas the similar IR spectrum of tenoxicam–sodium chloride coprecipitate could be the reason for the similar dissolution pattern to that of the parent drug.

Differential Scanning Calorimetry Studies

It was the general aim to prepare dispersions in which the drug was dispersed in as near a molecular state as possible to provide a thermoenergetic state of the drug of high aqueous solubility once the carrier dissolved. Thermal analysis, especially DSC, has proved a powerful tool in evaluating the drug-carrier interactions (11). DSC is particularly useful in determining the solubility of a drug in a polymeric carrier and is capable of detecting polymorphic modifications. Interactions in the samples are derived or deduced from DSC by changes in thermal events such as elimination of an endothermic or exothermic peak or appearance of a new peak (12). As shown in Figs. 9–14, the DSC thermogram of tenoxicam is characterized by an endothermic peak at 221°C, followed by an exothermic peak at 224°C. Examining the DSC thermograms of the different coprecipitates, it is clear that these characteristic peaks of the drug disappeared in the thermograms of all coprecipitates except for those prepared with sodium chloride. In the case of the coprecipitate prepared using sodium chloride, only a very slight shift in the peaks occurred, with the endothermic peak shifted from 221°C to 220°C and the exothermic peak shifted from 224°C to 223.6°C. This consistent thermogram of the coprecipitate with that of the drug indicates no structural changes in the coprecipitate and is similar to that obtained in the IR study, for which again the spectra of the sodium chloride coprecipitate was consistent with that of the parent drug.

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