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Recrystallization after powder compaction

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Summary

Scanning electron microscopy has been used to examine compacts of aspirin (ASA), anhydrous calcium gluceptate (CaG), $FeSO_4 \cdot H_2O$, metoclopramide hydrochloride (MCP), methenamine (MTA) and sucrose (S) prepared on a single-punch tablet press using both unlubricated and lubricated dies. The materials were directly compressible and included solids which exhibit plastic deformation and brittle fracture on compression. Surface recrystallization and changes in the matrix of the compact were observed after storage at 25°C and 0% RH and 43% RH. Crystal growth rates were particularly dramatic for ASA, CaG and MCP, where extensive surface recrystallization was observed within 60 min of compression. Recrystallization of MCP and MTA led to complete reorganization of the surface. Unlike the other solids, the surface of MTA compacts depended on lubrication. The surface of a lubricated compact was initially smooth, but without lubricant, it was highly disordered. After about 8 days and considerable structural reorganization, no significant difference remained between MTA compacts prepared with or without lubrication. Recrystallization occurred much more slowly with S and $FeSO_4 \cdot H_2O$, but surface growth and restructuring of the surface were apparent after about 12 weeks. Examination of diametrally fractured compacts showed recrystallization at crystal interfaces within the compact. It is suggested that the activity of some solids increases dramatically on compaction, possibly through the creation of lattice

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defects at the crystal surfaces. The consequent decrease in free energy necessary to restore thermodynamic equilibrium could explain the observed crystal growth, and may be responsible for bonding between the particles.

Introduction

A recent report using scanning electron microscopy (SEM) to examine positive replicas of the pore structure of sodium chloride compacts and direct surface examination of the compacts, has revealed both interparticulate and surface recrystallization after storage at relative humidities (RH) ranging from 33% to 94% and ambient temperature. Above 33% RH, the crushing strength increased up to the critical deliquescent point of 76% RH and was correlated with the recrystallization process (Down and McMullen, 1984).

In this work, a variety of materials have been compressed into single component compacts on a single punch tablet press and the surface examined using SEM to determine whether recrystallization after compaction is a more general phenomenon.

Materials and Methods

Aspirin (BDH Chemicals), anhydrous calcium gluceptate (prepared from calcium gluceptate 3-1/2 hydrate (Pfanstiehl) by dehydration at 60°C in vacuo for 16 h), ferrous sulfate monohydrate (prepared by dehydrating ferrous sulfate heptahydrate (Fisher Scientific) to constant weight over a boiling water bath), methenamine USP (Fisher Scientific) metoclopramide hydrochloride BP (Secifarma), and sucrose (BDH Chemicals) were used.

Each crystalline material was compressed in a die using a Carver hydraulic press, and the sample surface examined by SEM as described by Down (1983) to determine whether consolidation caused mainly plastic deformation or brittle fracture.

The materials were dried at 40°C in vacuo and stored over phosphorous pentoxide in a desiccator before compression into tablets in a hand-operated Stokes Model A single-punch tablet press fitted with 13/32 in. diameter, round, standard concave punches. For each material, a given weight was hand-filled into the die cavity and the upper punch setting adjusted to give satisfactory compacts. The die and punch faces were either unlubricated or lubricated with a 5% w/v solution of stearic acid in chloroform. Sufficient time was allowed for the chloroform to evaporate before filling the die. After compression the compacts were carefully cleaned by suction and brushing and stored in an incubator at 25°C in desiccators either over phosphorous pentoxide (0% RH) or over a saturated solution of potassium carbonate (43% RH).

After various storage times, compacts were sputter-coated with gold and examined in the SEM (ISI-40 or ETEC Auto Scan) using secondary electron imaging with an accelerating voltage of 10 kV or 20 kV, respectively. The ideal procedure

would have been to examine the same area of a compact and to follow any changes in its surface with time. However, the metal coat interfered with the recrystallization process, and it was necessary to use a separate compact at each time interval.

Results and Discussion

The materials examined were directly compressible and included examples of solids which exhibit plastic deformation (aspirin and methenamine) and brittle fracture (metoclopramide hydrochloride and sucrose) on consolidation; the crystals

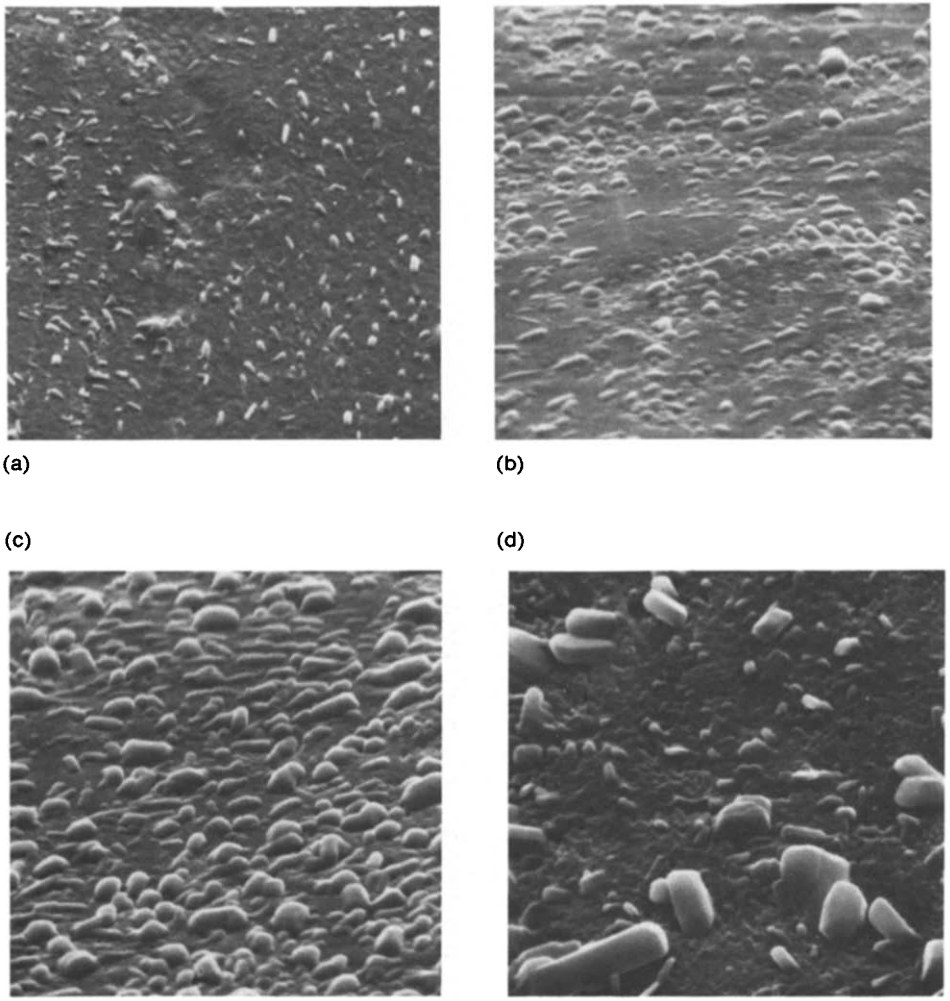

Fig. 1. Aspirin compacts after storage at 25°C and RH 0% for: (a) 15 min; (b) 6 h; (c) 24 h; and (d) 72 h. 4000×.

of anhydrous calcium gluceptate and ferrous sulfate monohydrate were too small to observe the process involved. Surface recrystallization and changes in the matrix of the tablets were observed for each material after storage at 25°C both at RH 0% and RH 43% showing, unlike sodium chloride, that atmospheric vapor pressure was not a factor in the process. Changes occurred whether the compacts were compressed in nonlubricated or lubricated dies; except where stated otherwise, the SEM micrographs in Figs. 1–5 are of lubricated compact edges.

Compacts of aspirin, anhydrous calcium gluceptate and metoclopramide hydrochloride showed crystal growth on the surface of the compacts within 60 min of compression. The rate of growth was particularly dramatic for aspirin, where crystals

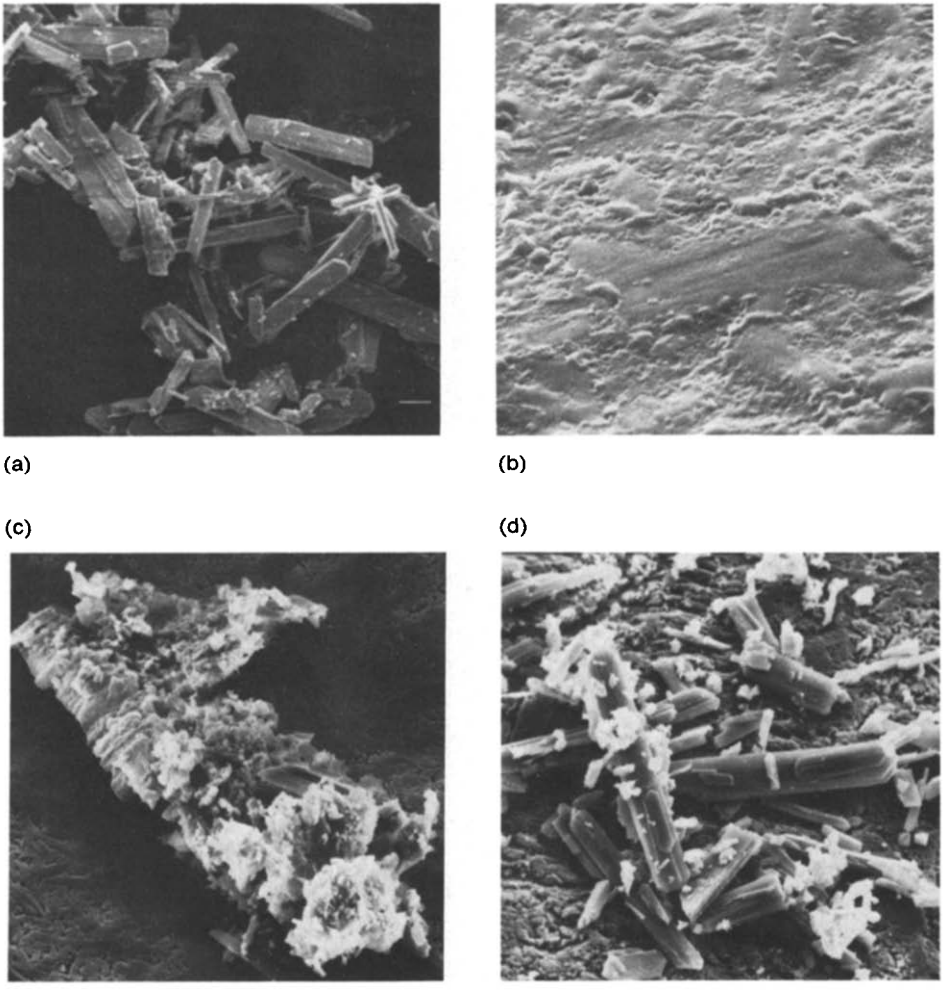

Fig. 2. Calcium gluceptate (anhydrous) (a) crystals; compacts stored at 25°C for: (b) 15 min, RH 0%; (c) 5 days, RH 0%; (d) 12 weeks, RH 43%. (a) 500×; (b) 4000×; (c) 1000×; (d) 800×.

were observed within 15 min, and showed an obvious increase in size and definition with time (Fig. 1). The rounded appearance of the aspirin crystals in the initial stages is characteristic of rapid growth, with the larger crystals apparently growing at the expense of the smaller ones. A reversible recrystallization on the surface of aspirin compacts has also been reported by Hess (1978), who attributed crystal disappearance on storage to temperature fluctuations. In this work, the storage temperature was maintained at 25°C and the disappearance of smaller crystals and growth of the larger ones is attributed to a solid-state Ostwald ripening effect. Aspirin in aspirin, phenacetin and caffeine tablets undergoes decomposition in the presence of stearic acid (Ribeiro et al., 1955). Although there was no suggestion that

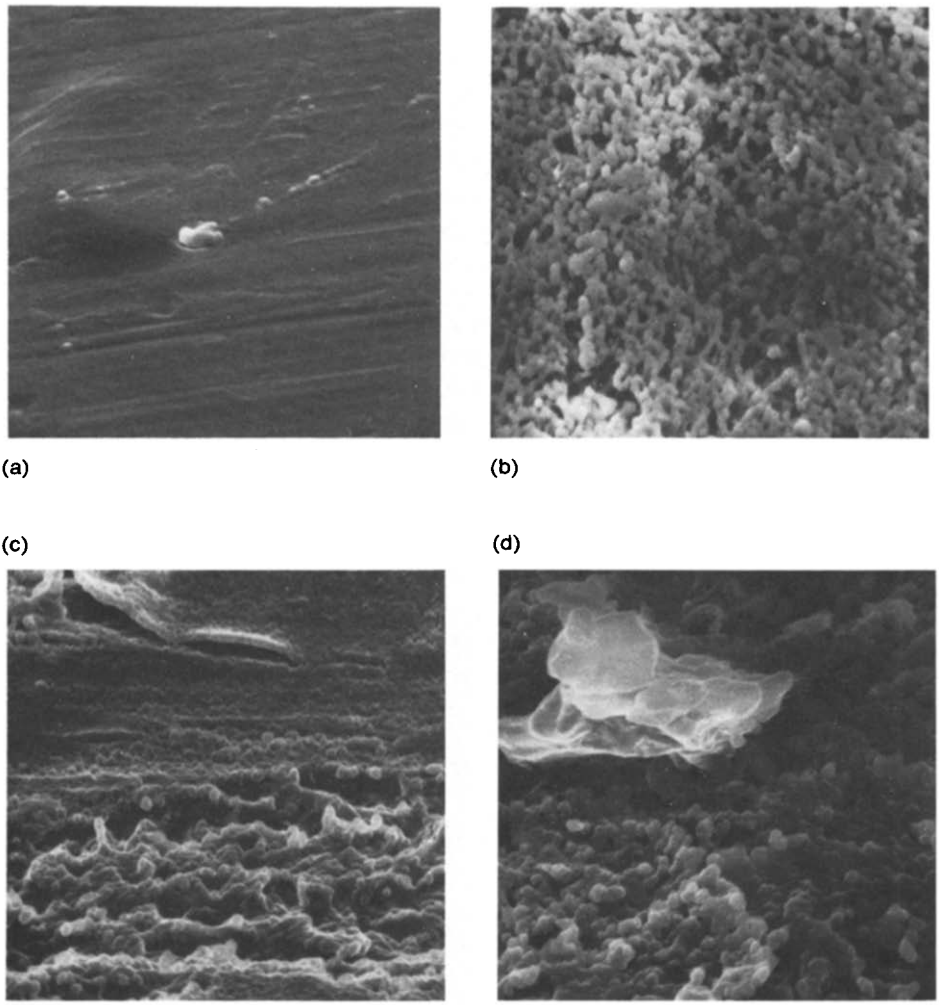

Fig. 3. Methenamine compacts after storage at 25°C for: (a) 40 min, RH 0%; (b) 40 min, RH 0% (no lubricant); (c) 24 h, RH 0% (no lubricant); (d) 8 days, RH 43%. 2000×.

aspirin decomposed in the presence of stearic acid alone, aspirin compacts were compressed in unlubricated dies and in dies lubricated with a solution of mineral oil in chloroform as well as with stearic acid. The nature and extent of crystal growth was similar for compacts compressed without lubricant and for both mineral oil and stearic acid, showing that the phenomenon was not related to the nature of the lubricant.

The surface of compacts of anhydrous calcium gluceptate was initially smooth and without obvious structure, but dendritic growth was apparent within 60 min, followed by extensive recrystallization both in the matrix and on the surface, where the crystal habit eventually became identical to that of the starting material (Fig. 2a–d). In contrast to the surface recrystallization observed after compressing anhydrous calcium gluceptate, aggregation but not recrystallization was observed after grinding this material for 2 h in a mechanical pestle and mortar. The nature of the shear stress and the proximity of adjacent crystals is clearly of paramount importance in the recrystallization reaction.

Recrystallization of methenamine and metoclopramide hydrochloride led to complete reorganization of the surface structure (Figs. 3 and 4). Unlike the other solids, the surface of methenamine compacts was markedly dependent on lubrication. The surface of a lubricated compact was initially smooth (Fig. 3a), but underwent massive changes with time. Without lubricant, the surface was initially highly disordered with a characteristic granular appearance (Fig. 3b), which after storage for 24 h became more dense (Fig. 3c). After about 8 days and considerable structural reorganization and surface growth, no significant differences remained between compacts compressed in lubricated or non-lubricated dies (Fig. 3d).

Recrystallization occurred much more slowly with ferrous sulfate monohydrate and sucrose, but surface growth and restructuring of the compact surface were apparent after about 12 weeks storage (Fig. 5).

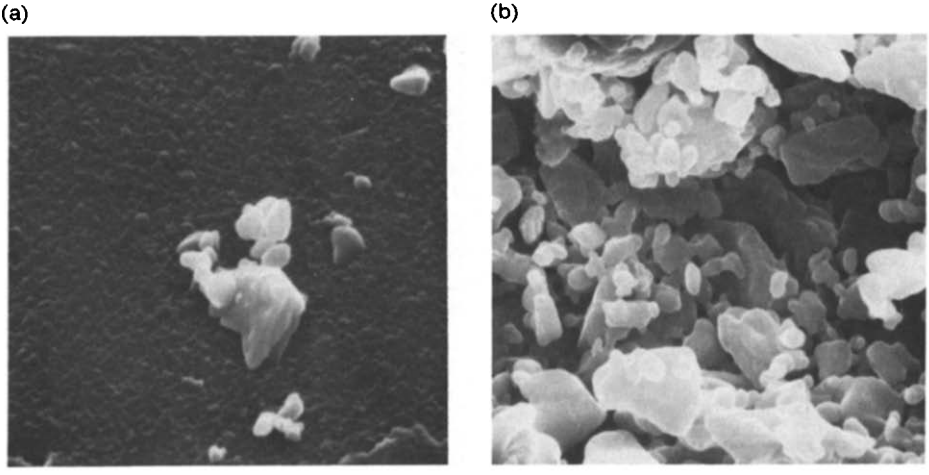

Fig. 4. Metoclopramide hydrochloride compacts after storage at 25°C and RH 0% for: (a) 5 h (no lubricant); (b) 8 days (no lubricant). (a) 4000×; (b) 3000×.

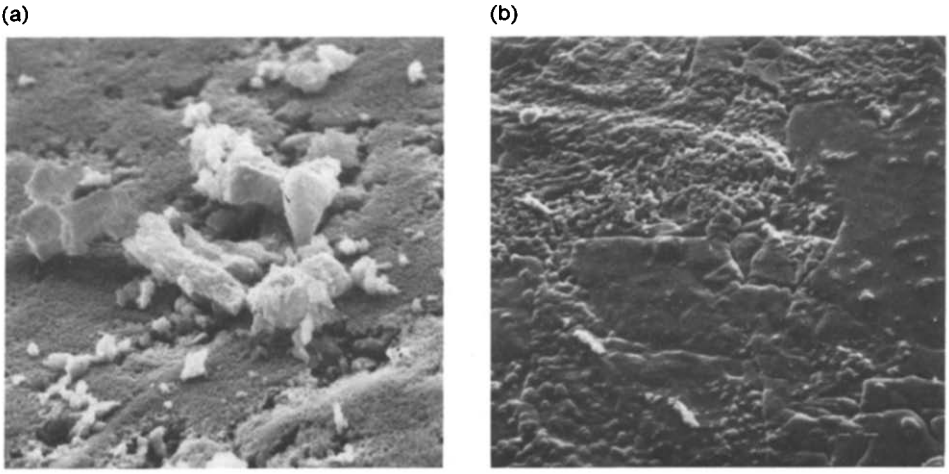

Fig. 5. (a) Dried ferrous sulfate compact after 12 weeks storage at 25°C and RH 43%. (b) Sucrose compact (face) after 6 months storage under ambient conditions. (a) 4000×; (b) 2000×.

Crystal growth occurred on both the edge and faces of the compacts, but was more extensive on the former, where there is greater frictional contact between the crystals and the die wall. Moreover, examination of diametrally fractured compacts showed recrystallization at crystal interfaces within the compact. The rate of recrystallization depended on the particular solid, but it is apparent that solid surfaces following compression are the locus of intense molecular activity. Recrystallization represents an increase in order in the system with a reduction in internal energy. By inference, compression creates a less stable disordered state at crystal-die wall and punch interfaces and at the interfaces between plastically deformed crystals. This process is the basis of the 'activation theory' of compact formation proposed by Huttenrauch (1978). Friesen et al. (1981) have shown that mechanical stress on single crystals increases the number of lattice defects. Compaction of crystals in a punch and die can be expected to produce an increase in the number of defects, particularly at crystal surfaces. Restoration to a more ordered state could explain the observed recrystallization and may be responsible for bonding. It is suggested that bonding results from an immediate dissipation of part of the energy imparted to the powder during compaction, while recrystallization is evidence for a slower restoration of thermodynamic equilibrium.

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