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**Short Communications**

# Mechano-chemical decomposition of drugs through galenic processes

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SUMMARY

A first example of chemical drug decomposition through the mechanical operations of grinding and compressing is described.

Since the discovery of the first mechano-chemical (tribo-chemical) reaction in 1892, numerous other reactions have been described that are induced by mechanical energy (Peters, 1962). We do not know, however, of any such descriptions being made in the field of drug formulation, where decomposition processes have so far been ascribed only to a thermal, photo-chemical or radio-chemical induction or, simply, to a low free activation enthalpy.

It seems logical, however, to assume the presence of mechanically induced reactions also in pharmaceutics (Hüttenrauch, 1978), because galenic grinding and compressing processes and other mechanical operations imply an energy transfer on the solid and, as a result, a mechanical activation of this material. The mechanical energy, thus, is also likely to give rise, in addition to such frequently described phenomena as mechanolyses, mechanical transformations of one modification into the other and mechanical disturbances of the normal order, to a chemical reaction with foreign molecules.

As a first experimental model to confirm this hypothesis and to determine the increase of a hydrolytic decomposition through mechanical activation, we chose the still problematic acetylsalicylic acid. Tablets of 6 mm in diameter were formed from this substance at a pressure varying between 18 and 72 kN/cm$^2$, stored at 80% relative humidity and then analyzed by spectrophotometry at 10- or 20-day intervals. Finally, the results were compared with those for untreated acetylsalicylic acid stored under the same conditions.

The tablets showed no increased decomposition rate when compared with the control, untreated acetylsalicylic acid, neither immediately after preparation nor after 10 weeks of storage. The same results were obtained for effervescent tablets of acetylsalicylic acid and sodium bicarbonate (equal parts). In these cases, the mechanical activation had no influence whatsoever on the stability of the samples.

The results were different for an oxidation reaction. We chose trenbolone acetate

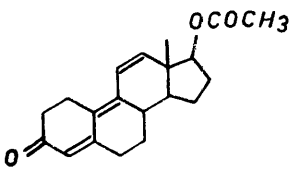
TABLE 1

DECOMPOSITION OF TRENBOLONE ACETATE (IN %) THROUGH GRINDING

| Auxiliaries | Duration of grinding | | |
|---|---|---|---|
| | 5 min | 20 min | 40 min |
| None | 0 | 3.68 | 3.53 |
| Lactose monohydrate [a] | 5.06 | 18.25 | 20.55 |
| Cellulose powder AVICEL [a] | 0 | 8.30 | 15.60 |
| Calcium biphosphate [a] | 0 | 3.55 | 2.50 |

[a] 2.5 g per 1 g trenbolone acetate.

(17β-hydroxy-4,9,11-estratriene-3-one-17-acetate), a steroid compound which, as a conjugated tetraene, is relatively sensitive to oxidation, to determine the effect.




*Trenbolone acetate*

Mixtures with PVP K 25 (at a ratio of 1 steroid : 2.5 auxiliary material) were tabletted at 65 kN/cm$^2$ to give compacts of 6 mm in diameter. The trenbolone acetate content was spectrophotometrically determined prior to, and after, tabletting. The result was a significant diminution through compression of 1.7%.

The next problem was to determine the influence of a grinding process. In this study, the active substance was ground by hand in a porcelain mortar for varying intervals of time both separately and in the presence of several auxiliaries (at ratios of 1 : 0.4 trenbolone acetate). The results are summarized in Table 1.

It is apparent from these results that the mechanical treatment does produce a decomposition. In two mixtures the decomposition of the trenbolone acetate rose significantly with the duration of grinding. The presence of tribochemical reactions in galenic operations can, therefore, be considered as established.

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