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Onset of the neutralising action of antacids based on calcium and magnesium carbonate using an artificial stomach model

An in-vitro study

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The in-vitro study evaluated the onset of the neutralising action of the antacid Rennie® as compared to a placebo. Among other things, the results showed a rise in the pH of the artificial stomach liquid from pH 1 to over 3 within 40 seconds after application of the antacid. The maximum pH of 5.24 was maintained over a period of approximately 10 minutes. At the same time, lower activity levels of mucosa-damaging pepsin were measured [3].

Reflux symptoms: a common ailment

Heartburn and acid reflux are widespread in the general population. In a Norwegian population-based study, approximately 40% of the test subjects reported suffering from reflux symptoms at least once a week [4]. If we transfer these results to the German population, it would mean there were around 33 million people suffering from reflux symptoms [1]. The antacid Rennie® has proved to be a rapid, effective, and safe tool in the symptomatic therapy of acid-related symptoms such as heartburn, acid reflux and a feeling of fullness. The calcium carbonate (680 mg) and magnesium carbonate (80 mg) it contains react with the stomach acid to form water and soluble mineral salts [3]. Through this reaction, the proton concentration is lowered. Although Rennie has been on the market for decades now, there are so far not many published studies investigating the onset of the neutralising action.

Investigating the neutralising effect

For testing purposes, the SHIME® apparatus (Simulator of the Human Intestinal Microbial Ecosystem, ProDiegest, Belgium) was used. This device models the individual compartments of the intestine, subdivided into stomach, duodenum, and colon. SHIME has been used extensively in the last 25 years and validated using in-vivo parameters. It constitutes an accepted scientific approximation of the human gastrointestinal tract. The artificial stomach contained 100 ml 0.1 N HCl and other important components such as mucins, salts (KCl, NaCl) and the reference protein bovine serum albumin (BSA).

For each test, two antacid tablets were incubated over the course of two hours and compared with two tablets of placebo. Each test was performed six times. The pH of the stomach liquid was measured every 15 seconds for the first five minutes and then, up until the end of the incubation time, every five minutes. The end point was the time until attaining a pH of 3.0, 3.5, 4.0, 4.5 and the maximum pH value, and the duration of the maximum pH value. The pepsin activity was determined indirectly via the fragmentation of BSA at the timepoints 0, 2.5, 5, 10, 15, 30, 45, 60, 90 and 120 minutes.

Following application of the antacid, the stomach acid secretion was simulated by a constant inflow of 3 ml/min 0.1 N HCl, and the emptying of the stomach by the constant drainage of 1.5 ml/min liquid. In addition, a homogenous environment was guaranteed in the container by means of a magnetic stirrer [3].

Results of the in-vitro study

For the antacid Rennie® it was shown that the pH (pH 1.0) increased to > 3 within 40 s (± 2 s) and was maintained for 56 min 1 s (± 1 min 9 s). After 1 min 54s (± 12 s), a pH of 4.5 was reached (**Fig. 1A**) and the maximum pH of 5.24 was attained within 10 min. This maximum pH was maintained for 9 min 56 s (± 44 s). Between 30 min and 1 h, the pH began to drop again (**Fig. 1B**). By contrast, the placebo only demonstrated a maximum increase to pH 1.28.

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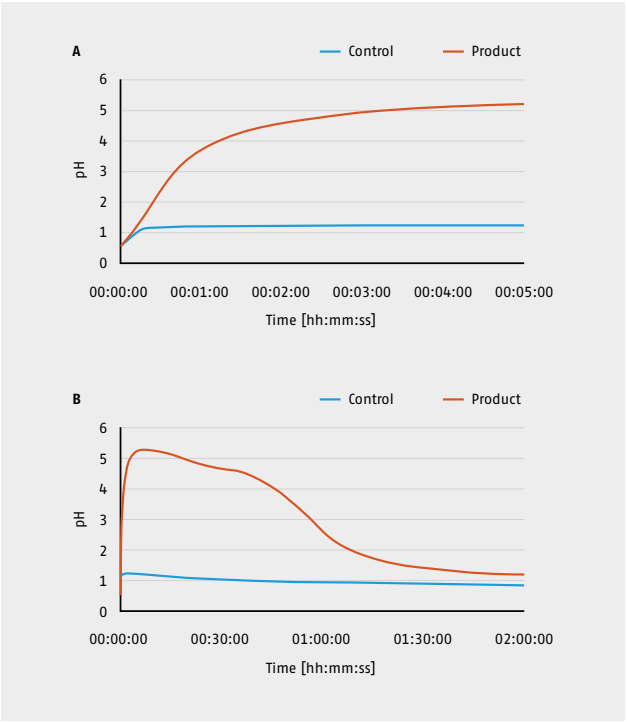

Fig. 1. Average pH profile of six independent repetitions of the incubation after addition of the calcium/magnesium carbonate-based antacid or placebo to the stomach medium. A. First 5 minutes of the incubation. B. Changes during the entire incubation time (2 h). Throughout the entire incubation, 0.1 N HCl was added at 3 ml/min, whilst the stomach emptying was simulated by removing the content at a rate of 1.5 ml/min.

The pepsin activity was reduced by the antacid, which is consistent with the rise in pH. With the placebo, a higher cumulative activity was measured over the entire period. However, the activity in the antacid trial after 1 h was higher than with the placebo. This is due to the approximated pH of 1.75, which constitutes the optimum pH for pepsin activity [3].

Summmary

Antacids based on calcium and magnesium carbonate have long been used for the symptomatic therapy of heartburn and acid reflux. In the in-vitro study it was shown that Rennie® significantly increases the pH of the stomach in less than a minute after application [3]. This is reflected in an observational study in which the test subjects reported an improvement in their symptoms after just five minutes [2]. Antacids exist as a good, and above all fast, alternative to proton pump inhibitors – which are significantly delayed in their onset of action – for the symptomatic therapy of intermittent heartburn.

Literature

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