

respectively by the compounds [(V-VIII)], [(III), (VI-X)] and [(III), (V-X)]. All these compounds save (IV) showed some inhibitory activity against any of the 3 test fungi. However, the compounds (IX), (X) and (V) showed specificity in their inhibitory action (Table I). The compounds (III), (IV) and (X) inhibited or disturbed the growth of germ tubes of the same fungus, allowing 80–100% germination of spores of *H. oryzae*. Germ tube growth was significantly reduced by these 3 compounds. Moreover, (III) and (IV) resulted in swellings of germ tubes (Table II). The compounds (VII), (III) and (VIII) were found to be highly potent growth inhibitors of all the fungi tested (Table III). Two of them (VII and VIII) appeared to be good germination inhibitors (Table I). Further, the compound (X) was found to be a specific inhibitor for *H. oryzae* alone. Differential growth inhibitory activity was shown by (V) and (IX), being inhibitory to all except *Rh. nigricans*, and by (IV), being inhibitory to all except *A. niger*. Sporulation inhibitory activity towards *H. oryzae* and *A. niger* was observed in only (VIII). The compounds (III) and (V) showed antisporulant activity for *H. oryzae* while (VI) and (X) exhibited the same property for *R. nigricans* (Table III). This is a very useful observation, since the importance of sporulation in secondary spread of such pathogens is very well-known<sup>9</sup>. The MIC for (VI) and (VIII) was

found to be 25 µg/ml and that for (VII) was 30 µg/ml. The high antifungal activity of these 3 compounds at such a low concentration is very promising. The compounds (III–X) appear to be somewhat broad spectrum in their activity towards different types of plant pathogenic fungi. Further, these types of chalcones and their corresponding dihydro and flavanone derivatives show fungitoxic property since most of them inhibited the fungi in different growth phases. Further work in this area is now underway<sup>10</sup>.

*Résumé.* Action antifongique et antisporulante de dérivés chalcones et flavones.

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## H<sup>+</sup> Secretion and Na<sup>+</sup>-K<sup>+</sup>-Dependent ATPase System in the Human Gastric Mucosa

H<sup>+</sup> secretion by the human stomach is one of the active cation transport processes<sup>1,2</sup>. During secretion the H<sup>+</sup> is concentrated 10<sup>6</sup> times against its concentration gradient in the stomach. It is well known that the H<sup>+</sup> secretion is an ATP-dependent process<sup>2</sup>. Two enzymatic ways are present for the hydrolysis of ATP at the level of the cell membrane: membrane ATPase system<sup>3,4</sup> and adenyl cyclase system<sup>5</sup>. Although both of the 2 systems were obtained in the human gastric mucosa<sup>6–12</sup>, the importance of these systems is unknown in the H<sup>+</sup> secretion.

In this paper, a positive and mathematically significant correlation has been proved to be present between the H<sup>+</sup> secretion and the Na<sup>+</sup>-K<sup>+</sup>-dependent ATPase activity from human fundic gastric mucosa.

*Material and methods.* In 45 patients with peptic ulcer (20 patients with gastric and 25 patients with duodenal ulcers), the H<sup>+</sup> secretion by the stomach was measured without application of any drug (basal acid output). The H<sup>+</sup> secretion was expressed in mEq/h. These patients underwent resection of stomach because of peptic ulceration. During operation a piece was cut out from the fundic part of the stomach. The gastric mucosa and the muscular layer were separated from each other and the membrane ATPase was prepared from fundic gastric mucosa with differential centrifugation (20,000 × g and 40,000 × g) and treatment with 2.0 M NaI solution according to the method previously described<sup>6</sup>. The membrane ATPase activity was measured in an incubation system at 37°C, by liberation of inorganic phosphorus<sup>7</sup>.

ATPase activity of membrane fraction from human fundic gastric mucosa

Mg <sup>2+</sup> -dependent ATPase	0.81 ± 0.13
Total/Mg <sup>2+</sup> -dependent and Na <sup>+</sup> -K <sup>+</sup> -dependent/ATPase	2.95 ± 0.10
Na <sup>+</sup> -K <sup>+</sup> -dependent ATPase	2.14 ± 0.11
Total + ouabain (10 <sup>-4</sup> M)	0.77 ± 0.13
Ouabain (10 <sup>-4</sup> M) inhibition	2.18 ± 0.12

The ATPase activity was determined in presence of 2 mM Mg<sup>2+</sup> (Mg<sup>2+</sup>-dependent part) and of 2 mM Mg<sup>2+</sup>, 80 mM Na<sup>+</sup> and 33 mM K<sup>+</sup> (total ATPase). Na<sup>+</sup>-K<sup>+</sup>-dependent ATPase was calculated as the difference between the total and Mg<sup>2+</sup>-dependent part alone. Ouabain was dissolved in the same salt solution (2 mM Mg<sup>2+</sup>, 80 mM Na<sup>+</sup> and 33 mM K<sup>+</sup>). ATPase activity was expressed as means ± SEM of 10 patients, in µmoles of inorganic phosphorus (P<sub>i</sub>) liberated by the transformation of ATP into ADP/mg membrane protein/h.

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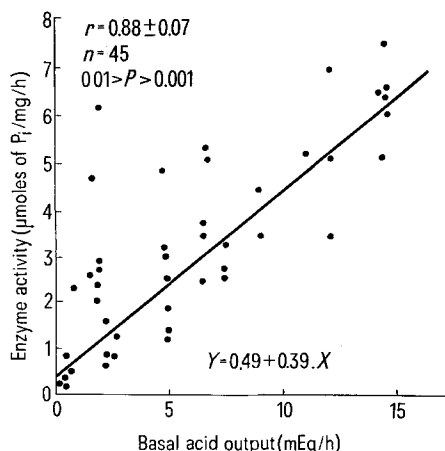
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Correlation between the  $\text{Na}^+\text{-K}^+$ -dependent ATPase activity from fundic gastric mucosa (ordinate) and  $\text{H}^+$  secretion (abscissa) in 45 patients ( $n$ ). Each single point represents the average of three different measurements.

The  $\text{Na}^+\text{-K}^+$ -dependent ATPase activity was calculated as the difference between the total (obtained in presence of  $\text{Mg}^{2+}$ ,  $\text{Na}^+$  and  $\text{K}^+$ ) and  $\text{Mg}^{2+}$ -dependent (obtained in presence of  $\text{Mg}^{2+}$ ) alone<sup>6-8</sup>.

**Results and discussion.** The Table shows the typical behaviour of membrane fractions from human gastric mucosa. The Figure indicates a positive and mathematically significant correlation between the  $\text{H}^+$  secretion by the stomach and the magnitudes of  $\text{Na}^+\text{-K}^+$ -dependent ATPase activity from human fundic gastric mucosa. The biological importance of this positive and significant correlation is as yet unknown between the above-mentioned parameters of the stomach. The energy utilisation from ATP for  $\text{H}^+$  secretion, by the way membrane ATPase system, is assumed by these results in the human fundic gastric mucosa.

**Zusammenfassung.** Es wurde bei Untersuchungen an 45 Patienten eine positive und mathematisch signifikante Korrelation zwischen der  $\text{H}^+$  Sekretion und der Aktivitätsgrösse der ATPase von Membrane der Fundusschleimhaut gefunden.

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### Inhibitory Effects of Dibutyryl and Cyclic AMP on the Compound Action Potential in the Frog (*Rana pipiens*) Sciatic Nerve

It has been reported that exogenous amounts of dibutyryl cyclic AMP and the methyl xanthines, theophylline and caffeine (which inhibit hydrolysis of cyclic AMP), were found to mimic the inhibitory effect of norepinephrine on Purkinje cells<sup>1</sup>.

The cerebellar Purkinje cell study, like many others, reports the influence of certain pharmacological agents on the synaptic process without regard to the effects these compounds may have on membrane excitability. It

should be kept in mind that drug modification of synaptic transmission may actually be a secondary outcome of the direct action of the compound on membrane excitability<sup>2</sup>.

In view of this consideration, this paper reports the effects of dibutyryl and cyclic AMP, as well as, theophylline and caffeine on various parameters of the compound action potential in the peripheral nervous system (frog sciatic nerve).

**Materials and methods.** Frogs (*R. pipiens*) were obtained from Mogul-Ed Biological Supply Co. After double pithing, the sciatic nerve was carefully dissected in isotonic Amphibian Ringer's (240 mOsm). All fascia and overlying branches of the sciatic artery were carefully removed with fire polished glass dissecting needles. Each nerve was severed just distal to spinal ganglia 7, 8, and 9, and proximal to its bifurcation of peroneal tibial components. The preparation was then removed and placed on electrodes in a nerve chamber into which air was bubbled at approximately 0.5 cm<sup>3</sup> min.

The basic design of this study was to expose the nerve tract to solutions of a) Amphibian Ringer's during dissection; b) test solution for 30 min; c) Amphibian Ringer's for 30 min to measure recovery. Following each of the three exposures, nerve characteristics such as chronaxie, spike amplitude, latency and conduction speed were compared. The test solutions were various concentrations of dibutyryl and cyclic AMP. Caffeine (0.2 mM) and theophylline (4 mM) were tested alone or in addition to dibutyryl and cyclic AMP. All data were ob-

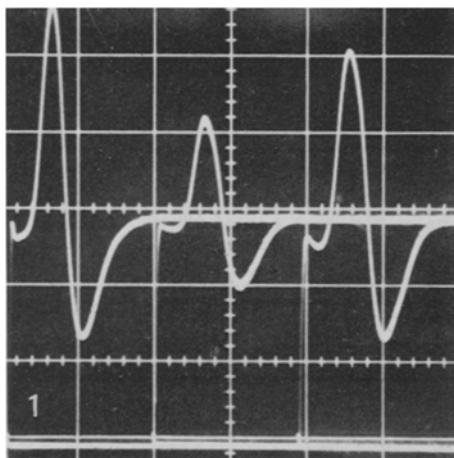


Fig. 1. First spike represents the inherent response to threshold stimulation. Second spike shows 14 mV decrease in response as result of 30 min exposure to  $1 \times 10^{-4}$  M cyclic AMP. Third spike indicates nearly complete recovery.

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