SHORT COMMUNICATIONS

INTERACTION OF CALCIUM AGONIST WITH SOME CARDIAC DRUGS

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THE antibiotics × 537 A and A 23187, which have been widely studied for their calcium agonistic properties, have been demonstrated to form lipophilic complexes with various cations and transport them across both biological and artifical membranes[1]. With the widespread involvement of calcium in biological systems, an induced transport of calcium across lipid barriers would be of considerable importance.

In the present study, the compound Ro–2–2985/001 (Lasalocid), a sodium salt of the antibiotic, ionophore × 537 A, a known calcium agonist[2], was tested for its effect on frog heart *in situ*, rabbit atria and isolated rabbit heart. It was used singly, and in combination with the cardiotonic drugs. All the observed effects have been presented in figure 1.

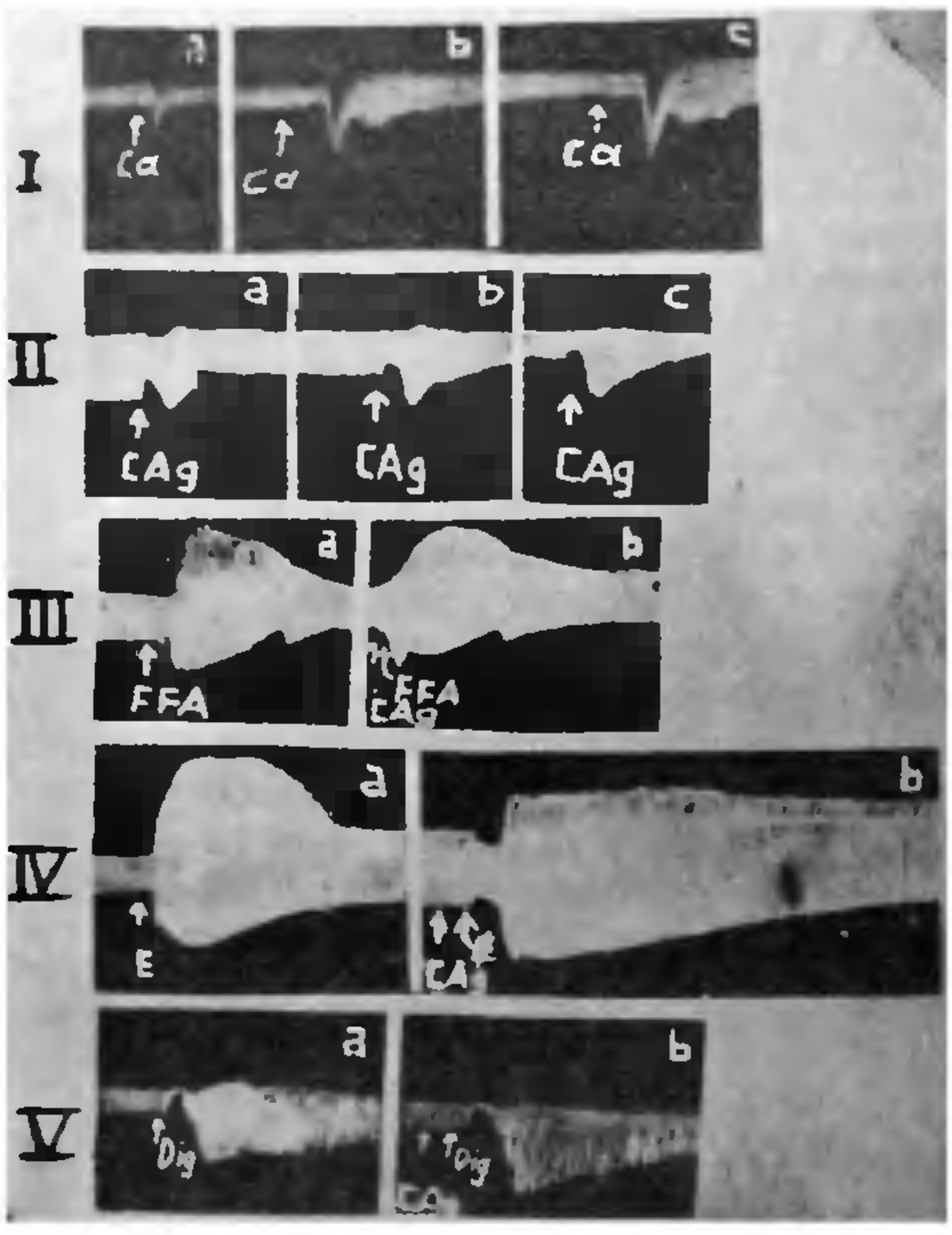

Figure 1. Calcium - Ca. (a) 3.17, (b) 6.35 and (c) 10.6 × 10^{-6} mol. **II.** Calcium agonist - C Ag. (a) 10 (b) 20 and (c) 30 μg. **III.** Free fatty acid - FFA. (a) 0.4 ml and (b) C Ag – 10 μg + FFA – 0.4 ml of a 4 mM solution. **IV.** Epinephrine - E. (a) 5.4 × and (b) C Ag - 10 μg + E – 5.4 × 10^{-7} moles. **V.** Digoxin - Dig. (a) 2.5 × and (b) C Ag – 10 μg + Dig – 2.5 × 10^{-7} moles.

The agonist produced a positive chronotropic and inotropic effect on the heart comparable to that produced by calcium (as $CaCl_2.2\,H_2O$, 6.35 × 10^{-6} mol), at a much lower concentration of the agonist (10–20 μg).

Administration of calcium agonist (10 μg), 30 sec prior to Epinephrine treatment (5.4 × 10^{-7} mol), significantly prolonged the duration of action of Epinephrine. The duration of action increased from 60% to 71.4%, as compared to the usual effect of Epinephrine. However, the rate of contraction of the heart (chronotropy), was only slightly affected. A very similar prolongation was also observed in Nor Epinephrine and Isoprenaline.

With the pretreatment of calcium agonist (10 μg), free fatty acid (0.4 ml of a 4 mM solution of sodium oleate) was able to produce cardiotonic effect of a much prolonged duration (62.5 to 73.6%). However, the calcium agonist failed to influence in any way the effects of Digoxin (2.5 × 10^{-7} mol) on heart.

Calcium agonists have been demonstrated to form lipid soluble complexes with divalent cations like calcium[1,3] and also Nor Epinephrine[3-5], and facilitate their transport across the lipid barrier. Therefore, it is conceivable that the significant enhancement in the duration of the cardiac stimulation due to catecholamines could be related with this phenomenon.

The cardiotropic effect of the agonist could not be observed by some workers in frog heart[2], which has been explained to be due to lack of catecholamine stores, in the heart of this species. However, not all effects of the agonist on different types of muscles are mediated by catecholamines, since a higher concentration of the agonist can increase intracellular calcium concentrations, possibly by increased calcium entry across plasma membrane, or release of calcium from sarcoplasmic reticulum, to evoke cardiotropic effect in frog heart[6,7].

Free fatty acids perhaps alter the membrance characteristics to augment electrolyte exchange and thus induce cardiotonic action[8]. Calcium agonist might act synergistically with free fatty acids, to prolong the duration of its cardiotropic effect.

Digoxin has no direct effect on calcium transport across the cell membrane. It has an indirect effect on net calcium enhancement in the cell, due to inhibition of Na^+-K^+-ATPase enzyme, and therefore the sodium pump[9,10]. It is obvious therefore that calcium agonist fails to influence the cardiac effects of Digoxin.

A significant prolongation of the cardiotropic effects of Epinephrine, while given in conjunction with the calcium agonist, could be of good clinical significance, especially during emergencies of cardiac crisis, like severe heart failure.

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THE FIRST RECORD OF THE GENUS *SPHAEROCHARA* (CHAROPHYTA) FROM THE UPPER SIVALIKS IN THE NORTH OF CHANDIGARH

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THE present communication places on record for the first time the charophyte taxon *Sphaerochara* from the Pinjor Formation of Upper Sivaliks. The rock units of Upper Sivaliks exposed in the northeast of Chandigarh are famous for their rich vertebrate fossil wealth since the first half of the nineteenth century. The recent recovery of two significant cercopithecoids namely, *Procynocephalus pinjorii*[1] and *Theropithecus delsoni*[2] has upgraded the deposits of this area to the category of palaeoanthropologically significant areas, which are very few.

Recently,during the systematic collection of fossil vertebrates, rock samples from different rock units of the area in the north of Chandigarh were collected by the authors for micropalaeontological investigations. The greyish siliceous clay from two localities, about 6.5 km and 9 km in the north of Chandigarh yielded a large assemblage of charophyte gyrogonites in association with freshwater gastropods, ostracodes and siluroid fish. The fossiliferous clay stratum, which yielded these microfloral remains, lies at the base of a local section and is overlain by alternating units of brownish yellow clay and yellowish grey medium to coarse-grained sandstone.

The assemblage of charophyte gyrogonites revealed, among others, about 150 specimens of *Sphaerochara*. Though charophytes from this area have earlier been recorded by other workers[3-5],the genus *Sphaerochara* remained hitherto unreported . Apart from being the first report from Upper Sivaliks, the present find is stratigraphically significant. Earlier, *Sphaerochara* was known from Lower and Middle Sivaliks only. The

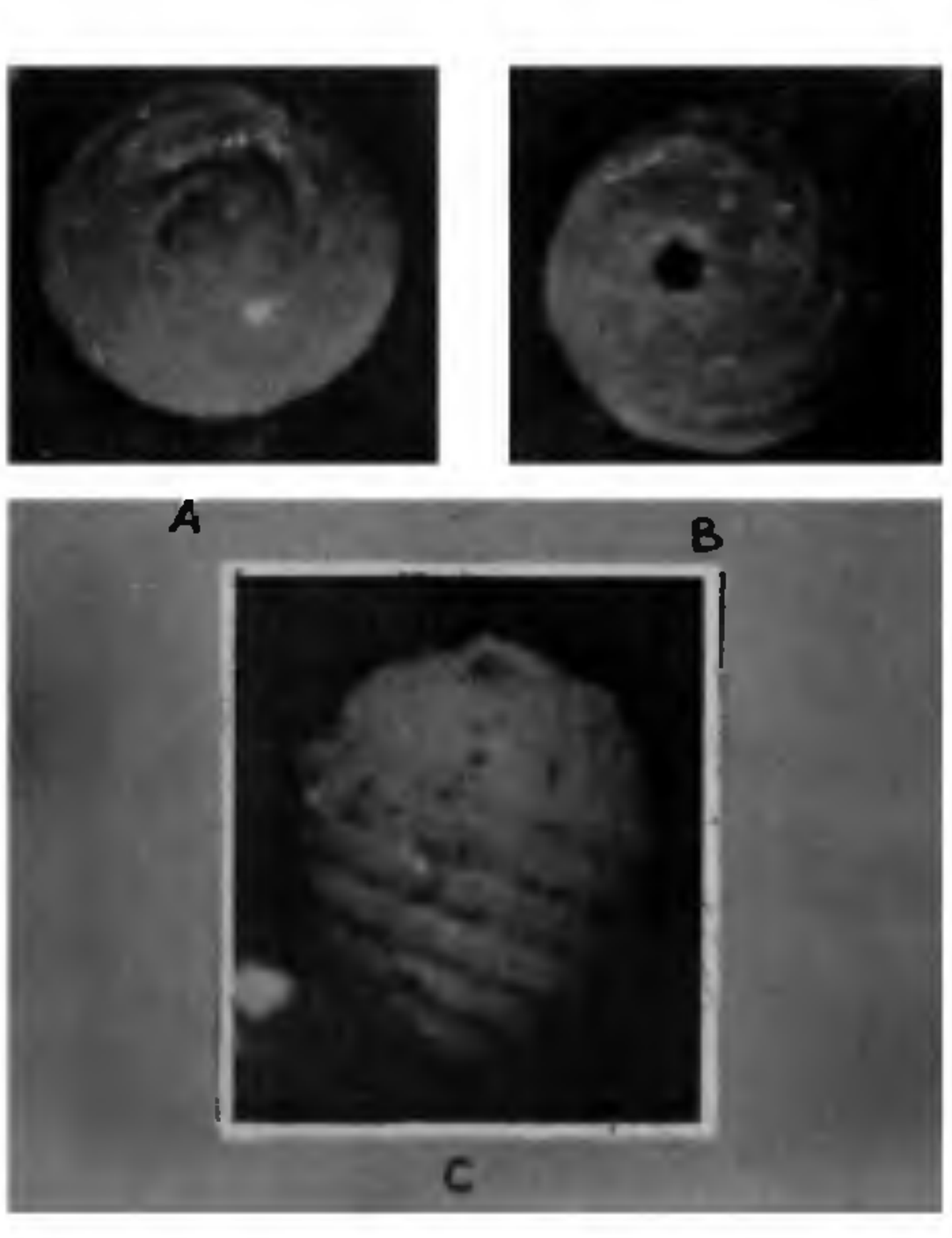

Figure 1. *Spaerochara* sp. from Upper Sivaliks. (A) Apical view; (B) Basal view; (C) Lateral view. (All figures approximately ×65).