portant role in these interactions. The greater the affinity of the compound for the lipids of the target membranes, the higher its antiarrhythmic activity.

Meanwhile, the other group of compounds consists of three preparations did not obey this rule. Possibly their very high affinity for lipids may have caused these substances to interact in the body not only with target membranes, but also with other lipid systems. As a result, the substance is delocalized in the body, its effective concentration in the target organ falls, and its aniarrhythmic activity is reduced correspondingly.

These results indicate that model phospholipid membranes can be used for the screening of pharmacological activity of heterocyclic compounds.

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POSSIBILITY OF PHARMACOLOGICAL REGULATION OF GASTROINTESTINAL MOTOR ACTIVITY

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The results of a pharmacological study of the effect of the gallate of the alkaloid cynoglossophine-heliosupine (cyngal), isolated from *Cynoglossum officinale*, on motor activity of the gastrointestinal tract are described. The substance was found to have high stimulating activity in both acute and chronic experiments on dogs, using balloon and electrographic recording methods. The stimulating action of cyngal on gastrointestinal motor activity can evidently be explained by the ability of the preparation to liberate serotonin from the bound state.

KEY WORDS: *motor activity of the gastrointestinal tract; pharmacology; serotonin; cyngal.*

Various methods can be used to influence the motor activity of the gastrointestinal tract when it is weakened: first, by the use of direct muscarinic (m) cholinomimetics, which excite peristalsis and increase smooth muscle tone through their direct effect on m-cholinergic systems of the digestive tract; second, by the use of anticholinesterase drugs, which facilitate the accumulation of endogenous acetylcholine and thereby maintain the level of nervous regulation. Third, the least studied method of influencing motor activity of the gastrointestinal tract is by the use of substances promoting the liberation of physiologically active substances from the bound, inactive state, e.g., certain sympatholytics [4] and liberators [1, 10].

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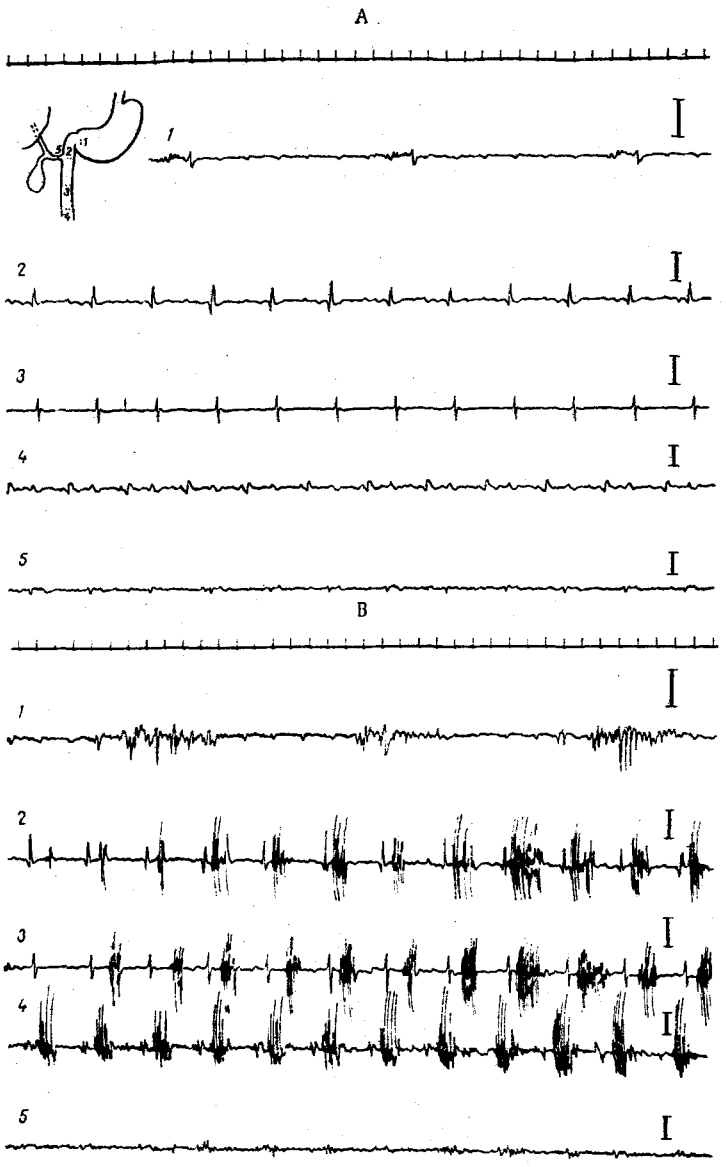

Fig. 1. Electrical activity of smooth muscles of digestive organs before and after injection of cyngal (1 mg/kg). A) Before injection of cyngal; B) 25 min after injection; 1) activity of antral portion of stomach; 2) activity of duodenum opposite Oddi's sphincter; 3) activity of distal segment of duodenum; 4) activity of jejunum; 5) activity of common bile duct in region of Oddi's sphincter. Calibration: 200 μV. Time marker 1 sec.

In the investigation described below the effect of the gallate of the alkaloid cynoglossophine-heliosupine (cyngal), isolated from the medicinal plan *Cynoglossum officinale* (Boraginaceae family), on the motor activity of the gastrointestinal tract was studied.

EXPERIMENTAL METHOD

Experiments were carried out on 7 mongrel dogs weighing 18-25 kg, 85 rats weighing 200.0 ± 40.0 g, and 10 cats. Gastric motor activity of the dogs was recorded by a balloon method through a Basov's fistula, intestinal activity by Thiry's method [5]. Bioelectrical activity of the smooth muscles of the stomach, intestine, and biliary tract was recorded under chronic experimental conditions by extracellular recording of potentials with implanted electrodes [8]. A radiological investigation of the motor function of the gall bladder was

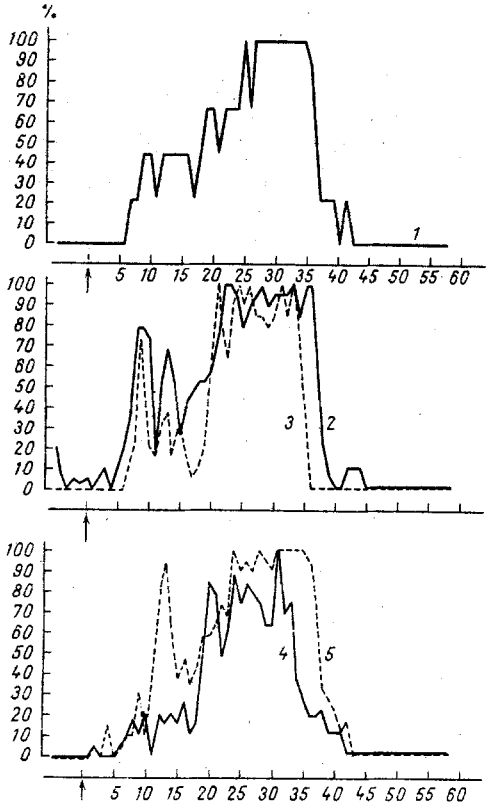

Fig. 2. Changes in electrical activity of smooth muscles of antral portion of stomach (1), proximal (2), and distal (3) segments of duodenum, common bile duct in region of Oddi's sphincter (4) and jejunum (5) after intramuscular injection of cyngal (arrow) in a dose of 1 mg/kg. Abscissa, time (in min); ordinate, ratio of slow waves containing spike potentials and total number of slow electrical waves per minute (in %).

carried out by means of the Diagnomax x-ray apparatus (Hungary) (voltage 69 kV, current 300 mA, exposure 0.12 sec). Radiological verification of the activity of the biliary system was obtained by excretory cholecystography using a 20% solution of iodipamide. Motor activity of the gastrointestinal tract was recorded (by balloon and electrographic methods) at a period of relative rest of the smooth muscles of the tract and 20 h after taking food. The serotonin concentration in the blood plasma, the mucous membrane of the small intestine (10 cm caudally to the ligament of Treitz), and of the stomach (the greater curvature) was determined by the ninhydrin test method [6]. The effect of drugs blocking D-, M-, and T-serotoninergic receptors on the action of cyngal was determined in acute experiments on cats in which the movements of the small intestine were recorded [3, 7]. The LSD substitute, BC-105 (Sandoz), in a dose of 0.05 mg/kg, was used to block D-serotoninergic receptors; morphine hydrochloride, in a dose of 0.1 mg/kg was used to block M-serotoninergic structures, and tipindole in a dose of 1.5 mg/kg to block T-serotoninergic receptors. The preparation of cyngal was injected subcutaneously into the dogs or given by mouth in doses of 0.5-2 mg/kg; it was given to rats intraperitoneally in doses of 1.5 and 10 mg/kg and to cats intravenously in a dose of 10 mg/kg.

EXPERIMENTAL RESULTS

The chronic experiments on dogs showed that cyngal stimulates motor activity of the stomach and intestine and enhances the bioelectrical activity of organs of the gastrointestinal tract and biliary system (Fig. 1), regardless of its mode of administration. The threshold dose of cyngal was 0.5 mg/kg.

After injection of cyngal in a dose of 1 mg/kg the number of slow waves containing volleys of spike potentials in the activity recorded from the antral portion of the stomach, the duodenum, and the common bile duct in the region of Oddi's sphincter was increased in the 6th minute. In activity recorded from the duodenum volleys of spikes appeared in the 3rd minute, and from the common bile ducts in the 5th-7th minite. During the first 18-20 min after injection of cyngal there was a gradual increase in electrical activity recorded from all the organs. The response to cyngal was maximal after 20-35 min (Fig. 2). At that time nearly all complexes of the basic electrical rhythm contained high-amplitude volleys of spikes of maximal duration. During the next 5-6 min a decrease in the number of slow electrical waves containing volleys of spikes and in the duration of the volleys of spikes themselves was observed, and they had completely disappeared after 45 min.

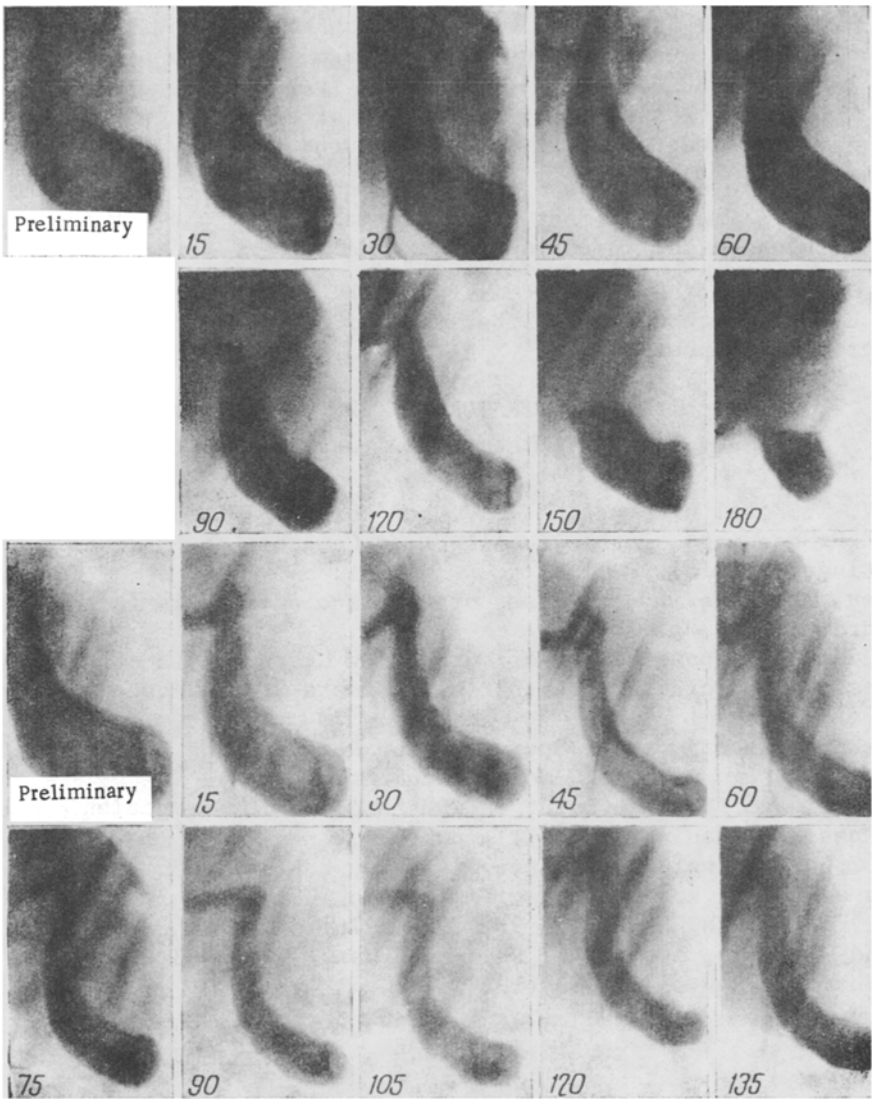

Fig. 3. Motor response of gall bladder during digestion and after injection of cyngal. A) During digestion (50 g raw egg yolks); B) after injection of cyngal, 1 mg/kg. Numbers show time in minutes.

Cyngal increased the outflow of bile from the gall bladder in the dogs, and this was accompanied by sharp contraction of the gall bladder walls. Emptying of the gall bladder after injection of cyngal took place twice as quickly as during digestion, as cholecystography showed (Fig. 3). Cyngal stimulated not only the electrical activity of the smooth muscles of the biliary system, but also the discharge of bile into the duodenum.

Recording of the movements of the duodenum by a balloon method showed that cyngal makes its contractions less chaotic and promotes orderliness of motor activity, a characteristic feature of several sympatholytics [4].

The study of the mechanism of action of cyngal showed that it possesses certain cholinominetic properties [2] and also the ability of liberating endogenous serotonin from the bound state. The increase in the blood serotonin concentration was directly dependent on the dose injected and it was accompanied by a simultaneous decrease in the content of this amine in the wall of the stomach and intestine. Statistically significant ($P < 0.05$) changes in the serotonin content in the blood and tissues were observed after injection of cyngal in doses of 5 and 10 mg/kg. For instance, 40 min after injection of cyngal in a dose of 10 mg/kg the plasma serotonin concentration rose from 0.21 ± 0.042 to 1.06 ± 0.19 µg/ml. Meanwhile the serotonin concentration in the intestinal wall fell from 6.7 ± 1.5 to 2.8 ± 0.7

μg/ml. In the stomach wall a considerable decrease in the serotonin concentration (from 6.8 ± 2.1 to 3.7 ± 1.8 μg/ml was observed 3 h after the injection of cyngal. The conversion of serotonin from the bound, inert state to the free state and liberation of the active amine into the plasma were accompanied by excitation of serotonin structures of the gastrointestinal tract, with a consequent stimulation of motor activity [9, 11].

Morphine hydrochloride and compound BC-105 did not change the action of cyngal, but tipindole prevented its stimulant effect. The sensitivity of the serotonin receptors to cyngal was restored 30 min after injection of tipindole.

Cyngal thus potentiates the motor activity of the smooth-muscle organs of the gastrointestinal tract, evidently through the liberation of serotonin from labile depots and excitation of T-serotonin receptors.

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