

Effects of *Hoelen* on the Efferent Activity of the Gastric Vagus Nerve in the Rat

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ABSTRACT—*Hoelen* is used to treat gastric disease in Eastern traditional medicine. The efferent activity on the gastric vagus nerve was studied in the rat, and the activity was found to increase after administration of *Hoelen* into the duodenum. In addition, we examined the effect of *Hoelen* fractions. Both the fraction containing polysaccharide and the triterpenoid-rich fraction increased activity significantly. *Hoelen* would thus appear useful for treating gastric disease by activating efferent activity of the gastric vagus nerve through the action of triterpenoid and polysaccharide.

Keywords: Vagus nerve, Gastric branch, *Hoelen*

Hoelen (*Bukuryo* in Japanese) obtained from *Poria cocos* Wolf (*Polyporaceae*), present in many Kampo medicines such as *Rikkunshi-to* and *Shikunshi-to*, is useful for treating chronic gastritis, edema, nephrosis, gastric atony, acute gastroenteric catarrh, nausea, emesis and dizziness. It is known that gastric function is regulated by the vagus nerve and total gastric and gastric mucosal blood flow increases when the gastric vagus nerve is stimulated (1–4). This study was conducted to determine whether an aqueous extract of *Hoelen* would increase the efferent activity of the gastric vagus nerve in rats. The effects of the active fraction of *Hoelen* on vagal efferent neural activity were also studied.

Male Wistar rats (Tokyo Laboratory Animals Science Corporation, Tokyo), weighing about 300 g, were used. They were maintained at controlled temperature, humidity and light with food and water available ad libitum. The animals were deprived of food for 18 hr prior to the start of the experiment and anesthetized by intraperitoneal injection of 1 g/kg urethane. All extracts of *Hoelen* were prepared as follows: Briefly, *Hoelen* purchased from a Chinese market, was extracted with boiling water to give the aqueous extract. Another sample of *Hoelen* was successively extracted with boiling methanol and then boiling water, giving a methanol solution (Fr. A) and a water solution (Fr. B). The methanol solution was filtrated to obtain the precipitate (Fr. C). The filtrate of the methanol solution was dissolved with a methanol-water mixture

(4:1) and successively partitioned with *n*-hexane and then chloroform to give the *n*-hexane fraction (Fr. D), the chloroform fraction (Fr. E) and the aqueous fraction (Fr. F), respectively. They were suspended in the vehicle (0.5% Tween 80/H₂O). Test drugs at doses of 200 mg/kg or vehicle were administered via a cannula inserted into the duodenum. Efferent nerve activity was measured by the method used by Nijjima et al. (5). After laparotomy, nerve filaments were dissected from the peripheral end of the ventral gastric branch of the vagus nerve, which originates from the ventral subdiaphragmatic vagus nerve trunk. The nerve efferent activity was recorded with a bipolar electrode of silver wire placed on the peripheral end of the gastric vagus nerve. Nerve activity was amplified by means of a condenser-coupled differential amplifier and displayed on an oscilloscope and stored on magnetic tape. All measurements were made following conversion of the raw data to standard pulses using a window discriminator by which nerve activity could be distinguished from background noise. A rate meter with a reset time of 5 sec was used to observe the time course of nerve activity recorded with a pen recorder. Efferent activity, which was monitored as the discharge rate before administration (impulses/5 sec), was evaluated at 30, 60 and 90 min following test drug administration. The data were evaluated by one-way of analysis of variance (ANOVA) followed by Fisher's protected least significant difference (Fisher's PLSD) test, with $P < 0.05$

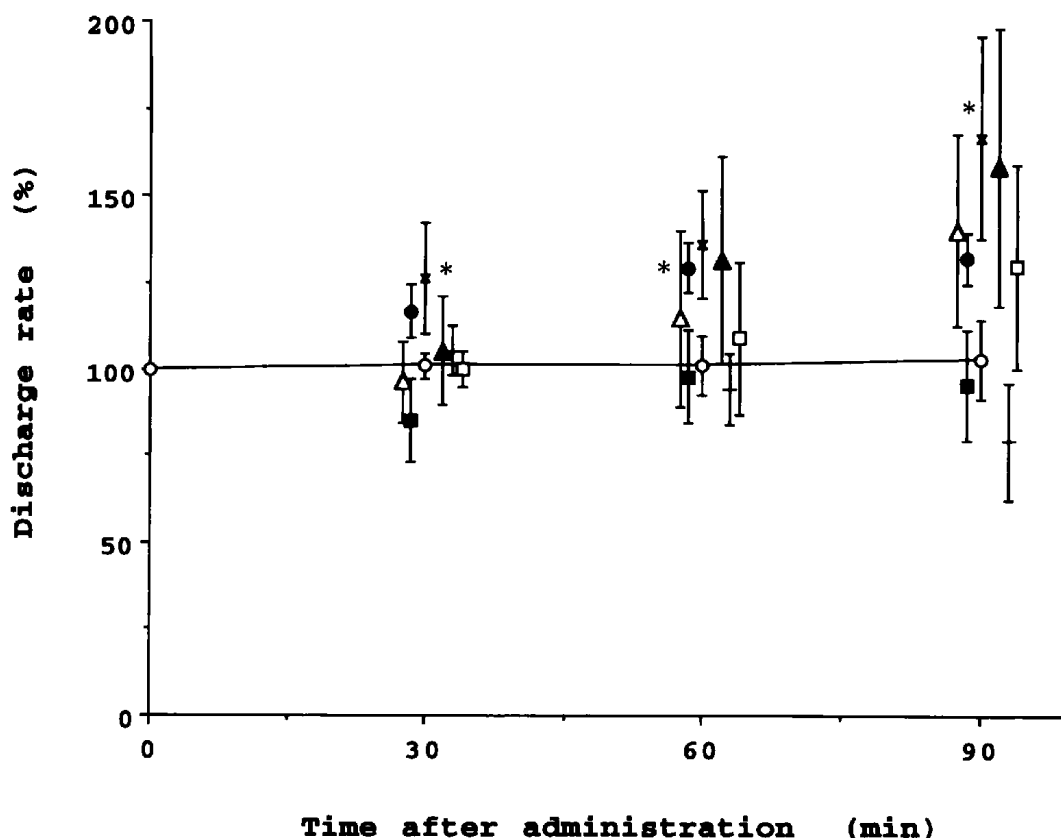


Fig. 1. Effects of *Hoelen* fractions on the efferent activity of the gastric branch of the vagus nerve. The values of vagal efferent neural activity are each given as means \pm S.E. of 4–9 animals. Symbols represent the following: —○—, vehicle (0.5% Tween 80); ●, aqueous extraction; △, Fr. A; ▲, Fr. B; □, Fr. C; ■, Fr. D; ×, Fr. E; +, Fr. F. (200 mg/kg, i.d.). Statistically significant difference from the control (vehicle) at * $P < 0.05$ by Fisher's PLSD.

regarded as significant.

As shown in Fig. 1, the aqueous *Hoelen* extract caused a gradual increase in the efferent activity of the vagus nerve, which reached a plateau (130%) from 60 to 90 min after administration. All *Hoelen* fractions, except Fr. D and Fr. F, gradually increased the activity, the mean value being about 130% at 90 min. Both Fr. B (polysaccharide-containing fraction) and Fr. E (triterpenoid-rich fraction) significantly increased nerve discharge. Typical records of the nerve activity are shown in Fig. 2. In general, activity gradually increased during the observations, and it was about 160% for both Fr. B and Fr. E at 90 min.

It is apparent from the present data that the aqueous extract of *Hoelen* increased the efferent activity of the gastric vagus nerve in rats. As prokinetic agents, cisapride (6), carpronium chloride (7) and aclatonium napadisitate (8) are used to treat chronic gastritis. Thus, *Hoelen* should be of use for treating gastrointestinal disease because of its parasympathomimetic effects. On the other hand, the polysaccharide included in *Pinellia ternata* Tuber has also been shown to increase the efferent activ-

ity of the gastric vagus nerve in rats (9). Therefore, *Pinellia ternata* Tuber may possibly act to facilitate gastric function due to its properties as a polysaccharide (5, 9, 10). Thus, the polysaccharide may also serve to regulate gastric movement in conjunction with the triterpenoids present in *Hoelen*. It is evident from the present findings that *Hoelen* should be applicable for the treatment of gastric disease by regulating gastric movement through its facilitatory effect on efferent discharge of the gastric vagus nerve.

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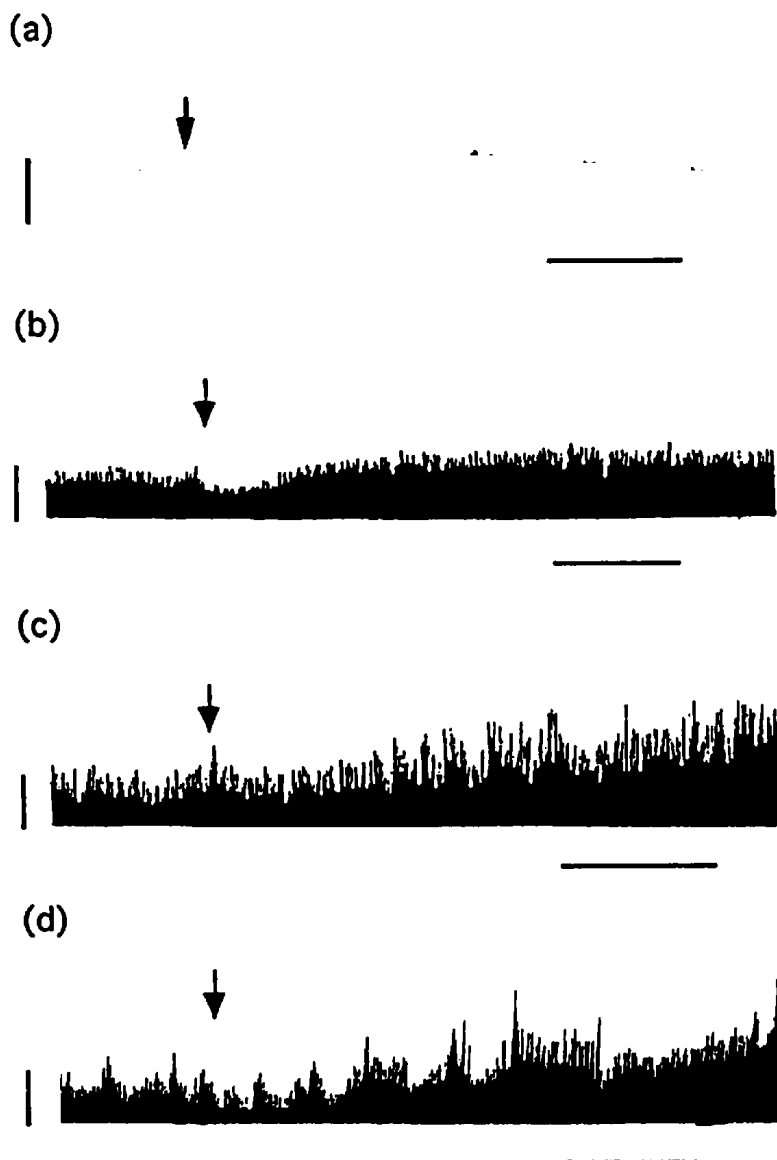


Fig. 2. Typical records show vehicle (0.5% Tween 80) (a), *Hoelen* aqueous extraction (b), Fr. B (c) and Fr. E (d). Each sample (200 mg/kg) was injected into the duodenum. The arrows show the administration time. Vertical bar: 100 impulses/5 sec. Horizontal bar: 30 min.

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