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Technical notes

Portable current stimulator for transdermal iontophoretic drug delivery

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ABSTRACT

A pulse stimulator was designed. It is small sized (3 × 2 cm printed circuit board) and battery-powered (185 μA total static current). The current intensity and pulse duration of this device can be continuously varied. Preliminary trials of lidocaine show that this device is usable for transdermal drug delivery and may be valuable for portable applications.

Keywords: Stimulator, iontophoresis, transdermal drug delivery

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INTRODUCTION

Transdermal iontophoretic delivery provides a means of noninvasive drug administration[1]. It has potential advantage for long-term medication whereas needle insertion may cause anxiety and pain. Further, it prevents possible degradation of peptide and protein drugs in the gastrointestinal tract as in oral administration[2]. However, due partly to the prerequisite of an accurately controlled current source that is minimized in size, this technique remains underexploited.

In this investigation we design a low-cost (<US$2), low-power, miniature stimulator for portable transdermal drug delivery. *In vitro* test has shown that the delivery rate can be controlled precisely by adjusting the current intensity and duty cycle of this device. Thus, this device is usable and might encourage the widespread use of transdermal iontophoretic delivery.

CIRCUIT DESIGN

Figure 1 shows the complete circuit diagram of the stimulator. For battery application, low-power design includes the use of low static current integrated circuits (ICs) and high impedance resistors and capacitors. This circuit is composed of a pulse generator and a voltage-to-current converter. Two CMOS timing chips (ICM7555) were used to provide a voltage pulse. The first one (IC1) was programmed as a frequency generator (astable multivibrator). The stimulation frequency is 1 kHz, which is determined by the 1.8 MΩ resistor, and the C1 capacitor. The pulse duration was controlled by the second chip (IC2), which was wired as a monostable multivibrator. The 200 kΩ variable resistor, the 200 kΩ resistor, and the C2 capacitor were used for adjusting the duty cycle from 5 to 50%. Following the pulse generator is the voltage-to-current converter, which involves 2 PNP transistors (2SA872) in current-mirror configuration. The 1 MΩ variable resistor was used to change the current intensity of the output pulse.

TRANSDERMAL DELIVERY

Results of *in vitro* delivery of lidocaine through rabbit pinna skins with this device are shown in *Figure 2*. Valia–Chien side-by-side diffusion cells and coiled platinum electrodes were used, and kept at 37±0.1 °C. Lidocaine concentration in donor solution (phosphate buffer, pH=7.4) was 2 mg/ml. During iontophoresis, 200 μl of receptor solution per h were taken for instantaneous analysis by capillary electrophoresis. For each sam-

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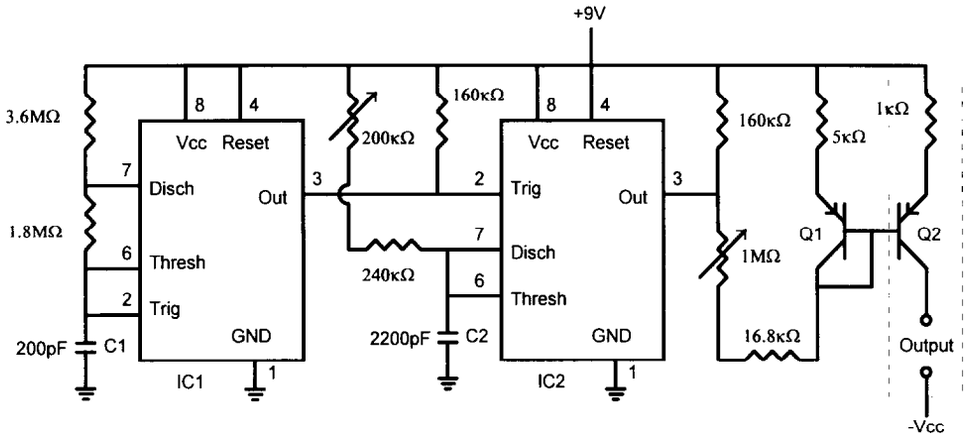

Figure 1 Circuit diagram of the stimulator

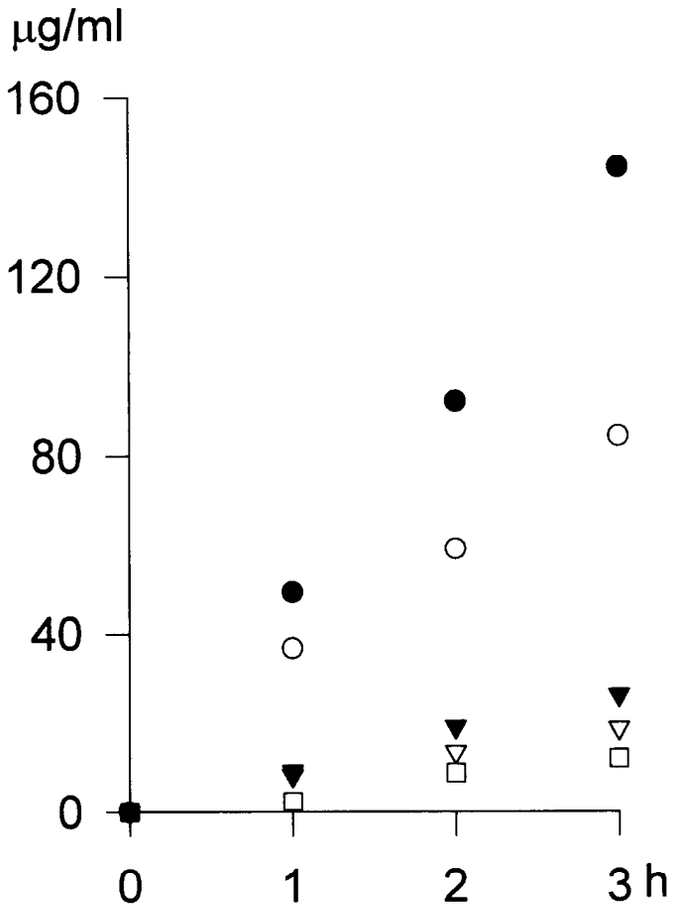

Figure 2 Results of transdermal delivery of lidocaine. Various symbols are used to represent iontophoresis conditions (current intensity and duty cycles) as follows: ● for 3 mA, 30%; ○ for 3 mA, 20%; ▼ for 0.5 mA, 30%; ▽ for 0.5 mA, 20%, and □ for control (no stimulation)

pling, 200 μl of fresh buffer was added back to keep the volume and osmotic pressure unchanged. In *Figure 2*, there are four trials with different pulse duration and current intensity of iontophoresis. The delivery rate was proportional both to the current intensity and pulse duration of the stimulation and remained constant in each trial. All the data obtained by iontophoresis were higher in concentration than the corresponding control data, which depend on the diffusion force alone.

DISCUSSION

The designed stimulator can be easily modified for different applications. We were able to change the frequency of stimulation and keep the duty cycle unaffected by changing the values of the C1 and C2 capacitors simultaneously by a 2-port-3-throw switch. Instead of the values shown in *Figure 1*, the C1 and C2 can be changed to 2000 and 22000 pF, respectively, for 100 Hz stimulation; and 33 and 470 pF for 5 kHz. For laboratory use, the Q2 portion (in the dotted rectangular box) can be duplicated for multichannel stimulation. Furthermore, the supply voltage ($-V_{cc}$) of the Q2 transistor can be increased up to 140 V for increasing the output compliance of the current source. For clinical use, either ground potential or −9 V is suggested for the $-V_{cc}$ to prevent any possibility of skin burns.

Considering the factors of low cost, miniature size, and safety (low supply voltage), we suppose that this device might find its way into user acceptance and might result in wide clinical applications.

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REFERENCES

1. Banga AK and Chien YW. Iontophoretic delivery of drugs: fundamentals, developments and biomedical applications. *J Controlled Release* 1988; **7:** 1–24.
2. Green P, Shroot B, Bernerd F, Pilgrim WR and Guy RH. In vitro and in vivo iontophoresis of a tripeptide across nude rat skin. *J Controlled Release* 1992; **20:** 209–18.