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[54] **APPARATUS AND METHOD FOR INDICATION OF IONTOPHORETIC DRUG DISPENSER OPERABILITY**

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[52] **U.S. Cl.** **604/20**; 128/783
[58] **Field of Search** 128/734, 783; 604/20

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,870,034 3/1975 James 128/734
4,109,645 8/1978 Bacchelli 128/734

OTHER PUBLICATIONS

S. Kaul, "Skin Resistance Biofeedback", *Elektor*, July/August 1980, pp. 7–29.

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[57] **ABSTRACT**

An iontrophoretic medical device has a first light of controlled brightness. Iontophoretic contact with skin is measured by current flow and a second light is illuminated in proportion to current flow. Generally, equivalent brightness of the two lights indicates successful iontophoretic contact.

4 Claims, 3 Drawing Figures

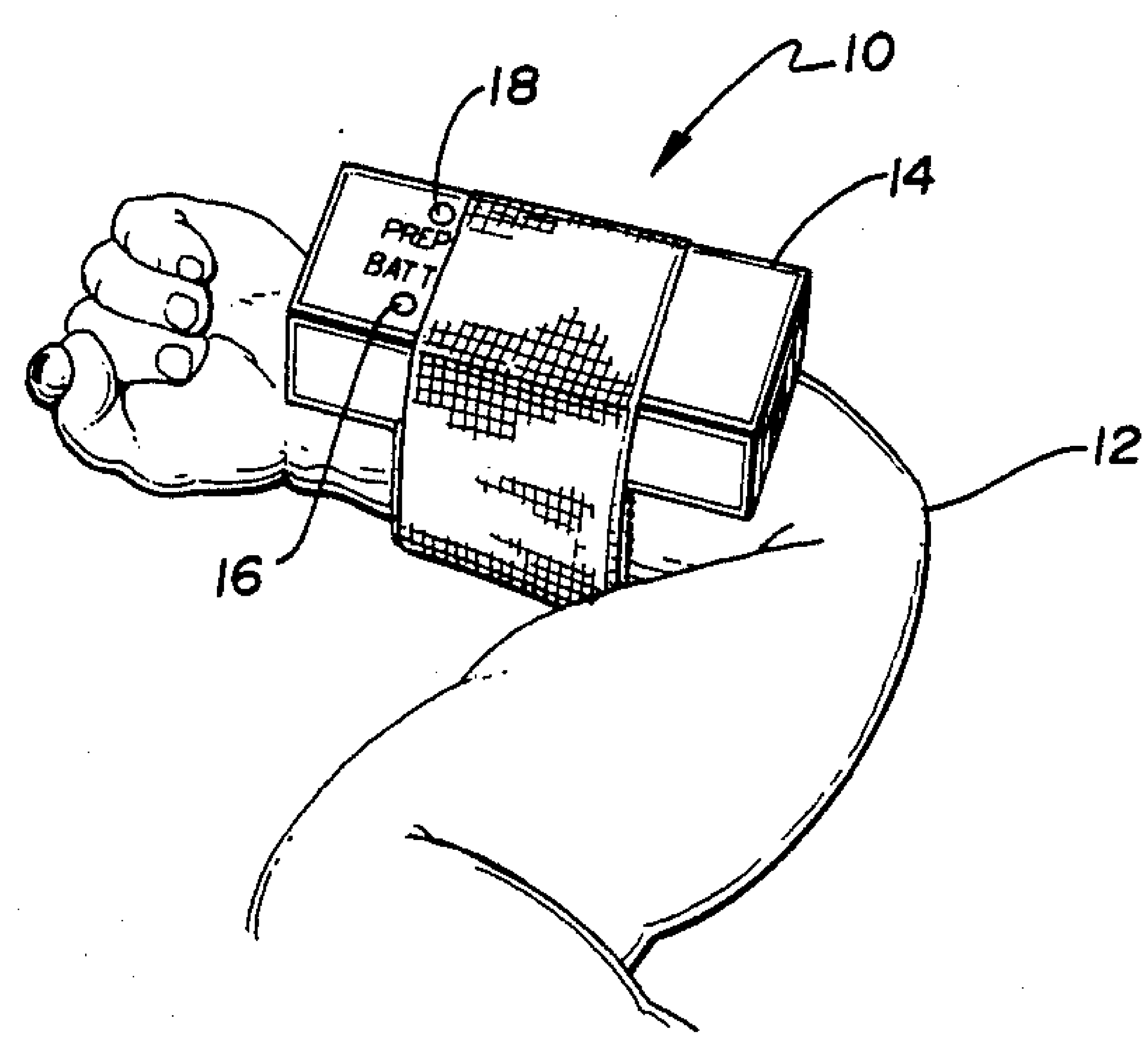


Fig. 1

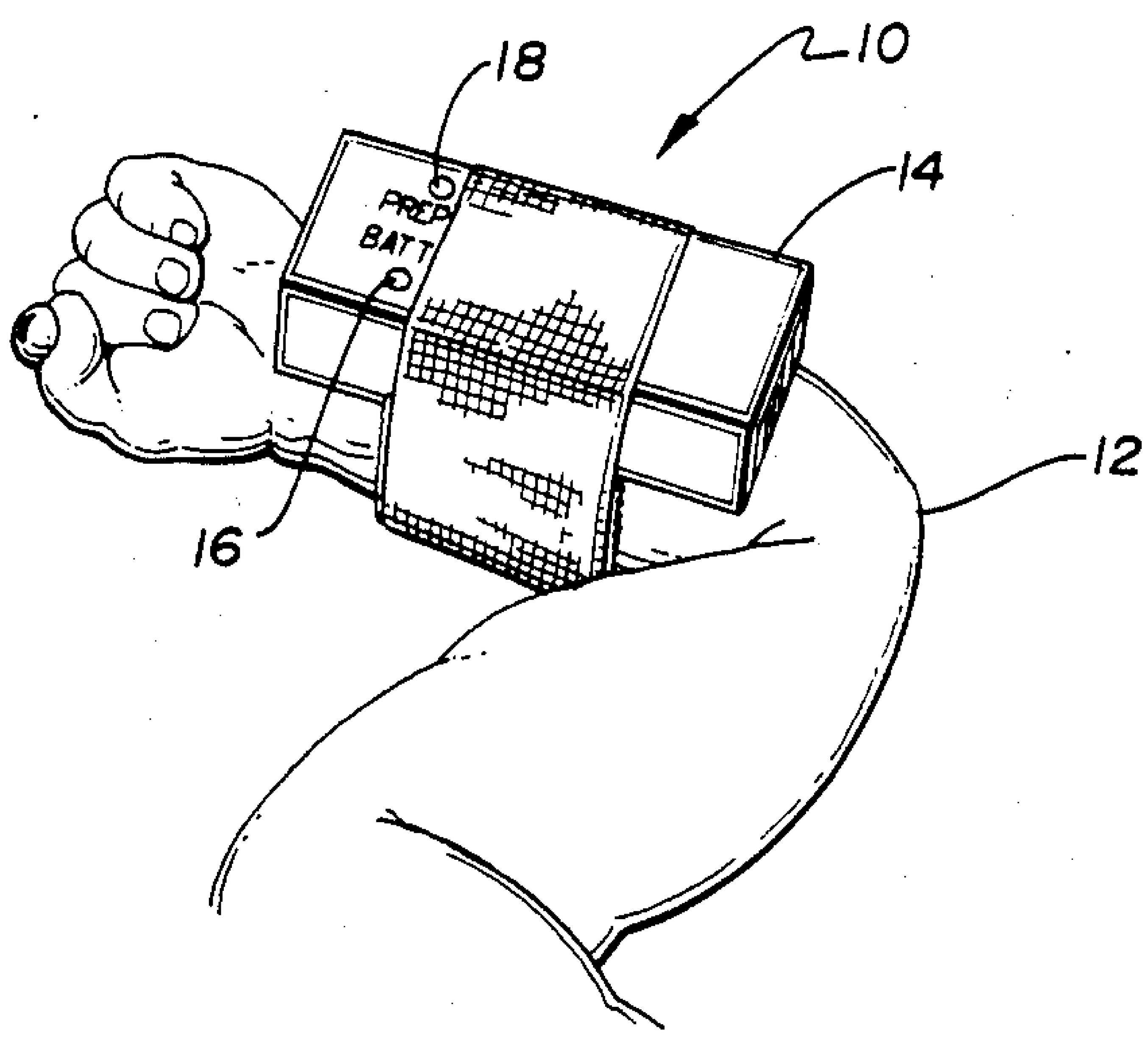
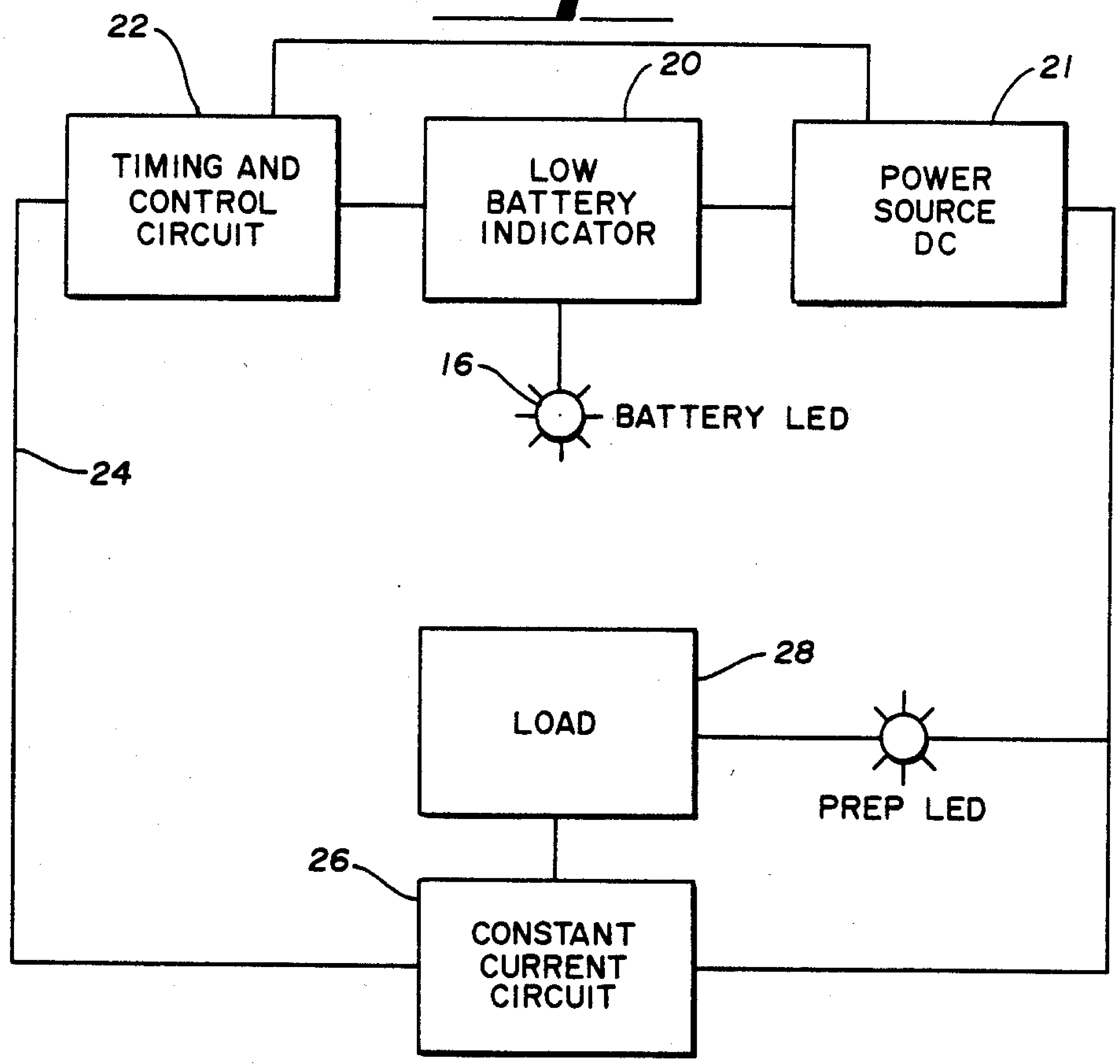

10
18
14
PREP
BATT
12
16

Fig. 2


22
20
21
TIMING AND CONTROL CIRCUIT
LOW BATTERY INDICATOR
POWER SOURCE DC
16
BATTERY LED
24
28
LOAD
PREP LED
26
CONSTANT CURRENT CIRCUIT

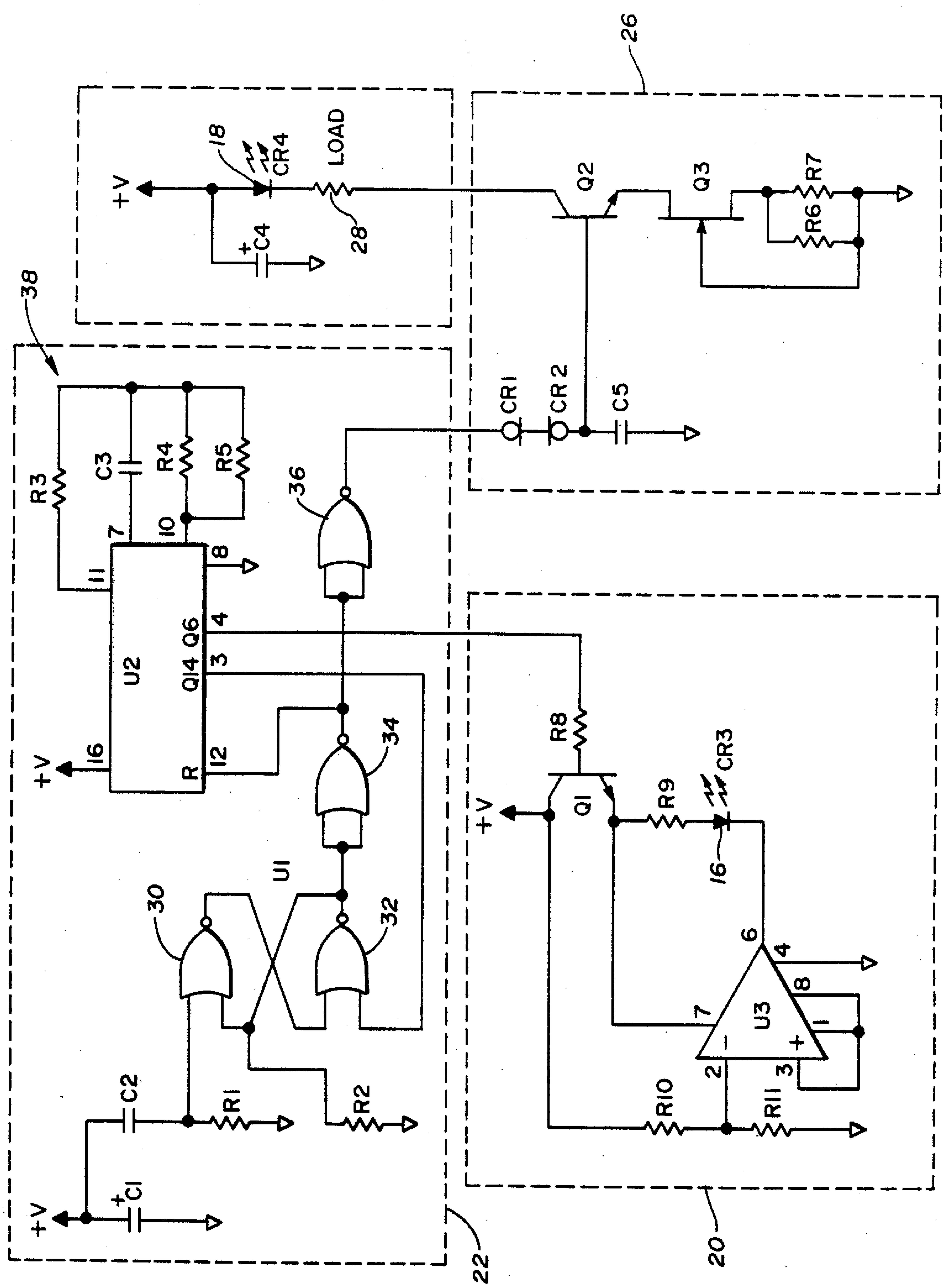

+V
18
CR4
LOAD
C4
28
26
Q2
Q3
R7
R6
38
R3
C3
R4
R5
U2
Q14 Q6
R
CR1
CR2
C5
36
34
U1
30
32
C1
C2
R1
R2
22
R8
Q1
R9
CR3
16
U3
R10
R11
20

Fig.3

APPARATUS AND METHOD FOR INDICATION OF IONTOPHORETIC DRUG DISPENSER OPERABILITY

BACKGROUND OF THE INVENTION

Field of the Invention—This invention relates to indicators for the degree of iontophoretic contact between iontophoresis device and the skin.

Priot Art—A number of devices have used iontophoresis for delivery of drugs through the skin. For example, the Medtronic CF indicator TM Sweat Test employs iontophoresis to drive pilocarpine to the skin to induce sweat. The sweat is used in the test for cystic fibrosis.

Practitioners using sweat test devices need an indication of when sufficient sweat is collected so that a test can be accurately conducted. Many factors can influence amount of sweat produced during the iontophoretic application of pilocarpine. One of the most influential factors is the impedance of the interface between the skin and the drug delivery electrode. Skin impedance varies from patient to patient depending on factors such as race, age, skin condition, or metabolic activity.

High skin impedance may often be dramatically lowered by a proper skin preparation, such as scrubbing. The degree of need for such extra scrubbing varies among individuals. If a test fails due to the need for greater skin preparation, it is advantageous to provide an indicator which will alert the practitioner to the need for additional skin preparation before the test is run.

Various methods have been tried to indicate to the operator the quality of the contact. For example, the model 417 Skin Chloride Measuring System produced by Orion Research includes an analog meter with a scale to indicate a zone of appropriate skin impedance which is to be achieved before beginning the manual timing of iontophoretic drug delivery. The needle on the meter is read by the operator to determine when the apparatus may be used.

U.S. Pat. No. 4,109,645 by Bacchelli discloses an instrument for measuring body resistance to ion flow after an established period which allows for the stabilization of skin impedance. This device also gives an analog meter reading for the assessment of impedance.

The analog meters are to cumbersome for quickly indicating to an operator of an iontophoretic device that proper skin preparation has been achieved. Such methods add to the circuit complexity and cost of the device. In the testing for cystic fibrosis, a simple indication is needed that sufficient sweat may be produced as the test is initiated.

SUMMARY OF THE INVENTION

An iontophoretic device constructed according to the present invention includes indicator lights to give a "go" condition indicative of sufficient iontophoretic contact. A control light is provided which serves a dual purpose. Illumination of the control light indicates that adequate power supply voltage is present to power the iontophoretic drug dispenser. Secondly, the control light, when lighted, provides a preset controlled brightness. Means are provided for iontophoretic contact with the skin. For example, this could be iontophoretic delivery of a drug. One example is the delivery of pilocarpine to generate sweat. Means are provided to sense the quality of the iontophoretic contact, preferably by sensing current flow across the skin impedance. Means are provided for determining whether current flow at the skin impedance is adequate. A second light is illuminated in a gradually brightening fashion to indicate the quality of the current flow. As current flow indicates that skin preparation is proper and iontophoretic delivery is achievable, a second light is illuminated to generally equivalent brightness to the control brightness of the first light.

The operator can easily determine by visual inspection of the first and second lights whether iontophoretic contact is sufficient. This indicator avoids the complex meter reading of the prior art systems and gives an indication which is easy to interpret. The operator of the device has an easy "go" or "no go" indication to use in deciding whether drug delivery is occurring in a satisfactory manner.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of an iontophoretic device having an indicator constructed according to the present invention;

FIG. 2 is a block diagram illustrating an embodiment of the present invention; and

FIG. 3 is a circuit diagram of the system of FIG. 2.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

A device **10**, as illustrated, includes indicator means constructed according to the present invention. Iontophoretic device **10** is illustrated mounted on a patient's arm **12** for iontophoretic delivery of a drug through the skin. The particular drug delivery device illustrated is a Medtronic® CF Indicator TM Sweat Test device which delivers pilocarpine as the first step in a test. On the housing **14** of device **10** are located a first LED or battery indicator light **16** and a second LED or prep light **18**.

The use of this sweat test device illustrates the present invention. The skin of the patient is prepared by washing. The device **10** is then strapped to arm **12** and activated. If there is sufficient power to drive device **10**, the first LED **16** lights up indicating that the device is operable. First LED **16** blinks on and off during iontophoretic drug delivery.

The physician employing device **10** then inspects second LED **18**. As current is conducted across the electrical load consisting of the patient's skin, second LED **18** is illuminated. If skin impedance is sufficiently low to allow proper operation of device **10**, second LED **18** is fully illuminated. The physican compares second LED **18** with first LED **16** to determine that skin impedance is sufficiently low to perform a test. If second LED **18** is dimmer than first LED **16**, the physician is warned that skin impedance many be too high to perform a successful test.

The normal procedure is then to remove device **10** from arm **12** and reprep the skin. This usually entails scrubbing the area to allow cleaner contact with device **10**. The device **10** is then restrapped to arm **12** and the procedure of comparing second LED **18** to first LED **16** is repeated.

The electrical circuit of device **10** is schematically illustrated in FIG. 2. Low battery indicator **20** includes circuitry for sensing voltage of power source **21** of device **10**. Low battery indicator **20** controls the illumination of first LED **16** and indicates that there is sufficient power to perform a test. Timing and control circuit **22** provides a control signal which is transmitted on line **24** to constant current circuit **26**.

Constant current circuit **26** provides the electrical current to perform iontophoresis on the skin of the patient which is represented by load **28**. The resistance across load **28** is in this example, the skin impedance of the patient. LED **18** is in series with load **28** so that its illumination depends upon the resistance of load **28**.

Details of the circuit illustrated in the schematic of FIG. 2 are shown in FIG. 3.

Timing and control circuit **22** comprises 33 microfarad capacitor **C1**, 01 microfarad capacitor **C2**, 1 megaohm resistors **R1** and **R2**, NOR gates **30** through **36**, 910 kilohm resistor **R5**, 560 kilohm resistor **R4**, 0.056 microfarad capacitor **C3**, 3.3. megohm resistor **R3** and ripple counter **U2**.

Capacitor **C1** is connected between ground and the positive 5 volt voltage terminal. This is a filter capacitor whose purpose is to reduce circuit noise, and is not otherwise actively involved in the timing control function. Capacitor **C2** is connected between the high voltage side of capacitor **C1** and the upper input terminal to NOR gate **30**, which terminal is also connected to ground through resistor **R1**. NOR gates **30** and **32** are coupled in a standard configuration for a flip-flop circuit. That is, the output of NOR gate **30** is connected to the upper input of NOR gate **32**, while the output of NOR gate **32** is connected to the lower input to gate **30**. The lower input to gate **32** is connected to the counter output **Q14** of ripple counter **U2**. The output of NOR gate **32** is also connected to the two inputs of NOR gate **34**. The lower input of gate **30** is also connected to ground through resistor **R2**. The output of NOR gate **34** is connected to the reset input R of ripple counter **U2** and also to both inputs of NOR gate **36**. Resistors **R4** and **R5** are connected in parallel between pin **10** of ripple counter **U2** and one side of capacitor **C3**, which is also connected through resistor **R3** to pin **11** of ripple counter **U2**. The other side of capacitor **C3** is connected to pin **9** of ripple counter **U2**. Pin **8** of ripple counter **U2** is connected to ground while pin **16** is connected to the +5 volt power supply. Ripple counter **U2** is a CD4060 ripple counter divider available from RCA Solid State Division, Box 3200, Summerville, N.J. 08876. The output of NOR gate **36** is applied to constant current circuit **26** which is described below.

When the device is activated, the inputs to NOR gate **34** will be at a logic "0" since they are connected to ground through resistor **R2**, and no current is initially flowing in the line. The output of gate **34** will thus be a logic "1" which resets ripple counter **U2**, setting the **Q14** output to a logic "0", and thus the lower input to gate **32** to a logic "0". At the same time a current will begin flowing in the circuit through resistor **R1** to ground (charge will be building on capacitor **C2**) which will set the upper terminal to NOR gate **30** at a logic "1". The output of gate **30** is thus forced to a logic "0" which is applied to the upper input of gate **32**. The two inputs to gate **32** being a logic "0", the output will switch to a logic "1". This causes the output of gate **34** to go to a logic "0", which releases the reset on ripple counter **U2**, which permits it to begin counting, and at the same time causes the output of gate **36** to switch from a logic "0" to a logic "1". While ripple counter **U2** is counting the upper input to NOR gate **30** falls to a logic "0", however the output of the gate is maintained at a logic "0" because the lower input to the gate is held at a logic "1" as long as the lower input of gate **32** is held to a logic "0".

Ripple counter **U2** is driven by oscillator circuit **38** consisting of resistors **R3**, **R4**, **R5** and capacitor **C3**. The value of resistor **R5** is selected so that the oscillation period is 36.6 milliseconds. The ripple counter will count the 36.6 milliseconds oscillations so that within approximately 5 minutes its fourteenth counter is triggered, and the **Q14** pin goes to a logic "1". This logic "1" signal applied to the lower input of gate **32** causes the output of the gate to go to a logic "0", which in turn forces the output of gate **34** to a logic "1", which holds ripple counter **U2** reset and changes the output of NOR gate **36** to a logic "0". The logic "0" output of NOR gate **32** is also applied to the lower input of NOR gate **30**. Both inputs of NOR gate **30** being a logic "0", the output will become a logic "1", which is applied to the upper input of NOR gate **32** forcing its output to a logic "0" thereby latching gates **30** and **32** in the "off" state such that the output of NOR gate **36** remains a logic "0" until the cycle is restarted. Thus, timing and control circuit **22** provides a logic "1" signal to constant current circuit **26** for a 5-minute period. While counter **U2** is counting up to five minutes, its sixth counter stage will go to a logic "1" approximately every 2.3 seconds: The output of the sixth counter stage (pin **4**) will thus go to a logic "1" for a 1.15 second period every 2.3 seconds. This signal is passed to low battery indicator circuit **20**. When the counter has fully counted the five minutes and gates **30** and **32** are latched into the "off" state all counter outputs will be at a logic "0" thus holding the various subcircuits in an off position as will be further described below.

Constant current circuit **26** includes two constant current IN5290 diodes **CR1** and **CR2**, 330 microfarad capacitor **C5**, 2N2222 transistor **Q2**, 2N4341 FET **Q3**, 680 kilohm resistor **R6** and 510 kilohm resistor **R7**.

The anode of constant current diode **CR1** is connected to the output of NOR gate **36** in timing and control circuit **22**. The cathode of diode **CR1** is connected to the cathode of diode **CR2** while the anode of diode **CR2** is connected to one side of capacitor **C5** and also to the base of transistor **Q2**. The other side of capacitor **C5** is connected to ground. The emitter of transistor **Q2** is connected to the drain of FET **Q3**. The gate of FET **Q3** is connected to ground and is also connected to its own source through parallel resistors **R6** and **R7**. The collector of transistor **Q2** is connected to load **28**.

When timing and control circuit **22** causes NOR gate **36** to go to a logic "1" state, a 5 volt signal is applied to the anode of diode **CR1**. Since this is a constant current diode the current that passes through it is fixed and thus the charge on capacitor **C5** is built up slowly, over a period of about 1 second. Thus, the voltage applied to the base of transistor **Q2** builds up slowly, to the full 5 volt value over the same period, causing the transistor to turn on slowly over the same period. FET **Q3** and resistors **R6** and **R7** form a conventional current-limiting circuit. Resistors are chosen to limit the current to 2 milliamps. Thus, upon application of the signal from timing and control circuit **22**, constant current circuit **26** slowly, over a period of about a second, ramps up the current through its output line from 0 to a maximum constant current of 2 milliamps. When, at the end of the 5-minute period, the signal from timing and control circuit **22** drops to a logic "0", the charge on capacitor **C5** will slowly drain through current-limiting diode **CR2**, again over about a 1-second period. Thus, the transistor Q2 will be slowly turned off over the same period and the current through the output line will slowly ramp down to a 0 value.

Low battery indicator circuit **20** comprises 100 kilohm resistor **R8**, 2N2222 transistor **Q1**, 2.2 kilohm resistor **R9**, LED **CR3**, an LM1OH differential amplifier **U3**, which is available from National Semiconductor Corp. at 29000 Semiconductor Drive, Santa Clara, CA 95051, 820 kilohm resistor **R10** and 12 kilohm resistor **R11**. The base of transistor **Q1** is connected to the **Q6** output (pin **4**) of ripple counter **U2** in timing and control circuit **22** through resistor **R8**. The collector of transistor **Q1** is connected to the positive 17 volt power source and to ground through resistors **R10** and **R11**. The emitter of transistor **Q1** is connected to the output (pin **6**) of amplifier **U3** through resistor **R9** and LED **CR3**, and is also connected to pin **7** of amplifier **U3**. The value of **R9** is selected such that the current passing through it is equal to a minimum desired iontophoretic current level, which is 1.5 ma in the preferred embodiment. Therefore, a current of 1.5 ma flows through LED **CR3** which causes **CR3** to provide a reference brightness to which the brightness of LED **CR4** is visually compared. The negative input terminal (pin **2**) of amplifier **U3** is connected to the line between resistors **R10** and **R11**. The positive input terminal (pin **3**) of amplifier **U3** is connected to both pin **1** and pin **8** of the same amplifier. The input pin **4** of the amplifier **U3** is connected to ground.

As discussed above, the **Q6** output of ripple counter **U2** in timing and control circuit **22** will go to a logic "1" for a 1.15 second period once each 2.3 seconds while the counter is running. Each time it goes to a logic "1" transistor **Q1** is turned on for the 1.15 second period provided the battery level is above the predetermined level which for this embodiment is 14 volts. The circuit consisting of amplifier **U3**, resistors **R9**, **R10**, and **R11** and LED **CR3** is a conventional battery-level test circuit disclosed in the applications manual for the **U3** amplifier published by National Semiconductor Corporation.

When transistor **Q1** turns on, it activates amplfier **U3** which compares the voltages between its negative and positive inputs. If the battery voltage is higher than 14 volts the amplifier connects its No. **6** pin output terminal to ground. This closes the circuit from the positive terminal to ground through LED **CR3**, causing the LED to operate. If the battery voltage is below 14 volts, amplifier **U3** will not connect its output (pin **6**) to ground and LED **CR3** will not turn on. Thus, Low Battery Indicator Circuit **20** will cause LED **CR3** to blink at 2.3 second intervals during the 5-minute period when the current is on, providing the battery level is above 14 volts.

Load **28** is illustrated as a resistor connected in series with constant current circuit **26**. PREP LED **18** (**CR4**) is connected in series between the load **28** and a 17 volt power source. A capacitor **C4** is connected from the 17 volt power source to ground.

The iontophoretic current flowing through load **28** is inversely proportional to the magnitude of the resistive impedance of load **28**. Since the load current must also flow through **CR4**, the brightness of **CR4** is therefore inversely related to the resistance in load **28**. A brightness of **CR4** less than that of **CR3** indicates current in load **28** of less than desired minimum (1.5 ma) and indicates that load impedance is undesirably high. Brightness of **CR4** equal to or greater than reference brightness **CR3** indicates that at least 1.5 ma iontophoretic current is being delivered to the load but not greater than 2.0 ma which is controlled by constant current circuit **26**.

The present invention is useful in the operation of any iontophoretic device, since overcoming skin impedance is a major problem in successful drug delivery. While the invention has been illustrated in terms of a test device which iontophoretically drives pilocarpine into the skin, it is to be understood that this embodiment is not limiting as to the scope of the present invention, but merely illustrative.

What is claimed is:

1. A medical device for making iontophoretic contact with skin of a patient comprising:
- a first visual indicator having a first controlled indication level;
- means for making iontophoretic contact with skin of a patient;
- means for measuring current flow across the impedance of the patient's skin;
- a second visual indicator;
- means for activating the second visual indicator to a indication level indicative of current flow across the impedance of the patient's skin, so that the indication level may be visually compared to the first indication level.

2. The device of claim **1** wherein the first visual indicator and the second visual indicator are lights.

3. In a medical device operating by iontophoretic contact with the skin, the improvement comprising:
- a first control light which is constantly illuminated to a control brightness;
- means for making iontophoretic contact with skin of a patient;
- means for measuring iontophoretic current flow across the impedance of the patient's skin; and
- means electrically connected to the means for sensing current flow for determining a level of satisfactory current flow; a second indicator light; and means responsive to the means for sensing current flow for illuminating the second light, such that a satisfactory level of current flow results in an illumination of the second light generally visually equivalent to the illumination of the first light.

4. A method of iontophoretic treatment of a human patient comprising the following steps:
- providing a device for making iontophoretic contact with the skin;
- providing a first light of a constant control brightness;
- providing a second light electrically connected with the device for iontophoretic contact such that brightness of a light indicates the quality of the contact with the skin;
- comparing the brightness of the second light with the brightness of the first light; and
- determining, based upon general equivalence of the brightness of the first and second lights that proper iontophoretic contact with the skin has been achieved.

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