MONITORING BLOOD GLUCOSE LEVELS

FIELD OF INVENTION

The present invention relates to apparatus and methods for the measurement of blood sugar concentrations and particularly, but not exclusively, to non-invasive *in vivo* measurement of blood glucose concentrations.

BACKGROUND

Traditionally, a person's blood sugar level is measured from a sample of blood obtained by a pin prick on the finger or drawn from the person's veins. A disadvantage of these methods is that they are invasive.

Various non-invasive techniques for monitoring blood sugar levels have been proposed.

International Patent Application Publication Nos. WO 0060350 and WO 0122871 describe a non-invasive optical sensor for measuring glucose concentrations in the eye. The sensor uses the magnetic optical rotatory effect (MORE) by which rotation of the polarisation of a light beam is dependent, in part, upon the concentration of a glucose solution through which the beam passes. A beam of polarised light is passed through the aqueous humor of the eye which is simultaneously exposed to a magnetic field. A photo-detector monitors rotation of the polarisation of the beam, from which is determined the glucose concentration.

International Patent Application Publication No. WO 0147415 describes non-invasive measurement of blood glucose. An RF signal is transmitted through a sample which is placed in a magnetic field between high-gauss permanent magnets. A concentration is determined from the reduction in the amplitude of the RF signal at a characteristic frequency.

International Patent Application Publication No. WO 0216910 describes a system for non-invasive monitoring of blood glucose. The monitor has a polarised light source for illuminating body tissue, and a magnetic field generator which creates a magnetic field within the tissue during illumination. The change in polarisation of light transmitted through the sample is used to determine a mean path length of photons through the sample. The mean path length is combined with spectroscopic measurements at various wavelengths to compute the blood constituent concentrations.

United States Patent No. 5,313,941 describes using a radiation source of long infrared energy, specifically from 2000 to 20,000 nm, applied in short bursts to avoid patient discomfort and/or burning of tissue. A wavelength of approximately 9100 nm is used to detect the concentration of glucose, and a wavelength of approximately 10,500 nm is used as a reference. The source of infrared energy is a heating element that radiates a broad spectrum of energy, and a mechanical shutter regulates the flow of energy into short bursts. The shutter is synchronized with the patient's systolic and diastolic phases of the cardiac cycle. A disadvantage of this method is that sophisticated filters and photodetectors are needed to measure the signals in these spectral regions. Another disadvantage is that the high energy source requires a large power supply, which restricts the ability to construct a compact and portable unit.

Experimental investigation involving the use of optics and photonics in other techniques for the non-invasive monitoring of blood glucose have shown promising results. Characteristic glucose absorption peaks at near infrared (NIR) wavelengths have been experimentally identified and reported.

United States Patent No. 6,097,975 describes the non-invasive measurement of blood glucose concentration using light pulses directed onto a patient's skin. Light reflected back is passed through light filters that transmit a narrow bandwidth of light within a range of wavelengths that is absorbed by glucose and then measured for use in determining the patient's blood glucose concentration. A suitable range of wavelengths said to be absorbed by glucose are identified as from about 1550 nm to 1700 nm and from about 2050 nm to 2400 nm, or more preferably from about 2080 to 2200 nm.

However, there are no commercially available devices for blood glucose monitoring utilising an NIR absorption technique. One main reason for this is the interference caused by other constituents and fluids in blood and in surrounding body tissue. Although the absorption of glucose in a simple pure solution exhibits various distinct peaks in the NIR band of the spectrum, there are chemical and biological constituents in blood and other body fluids and tissues that exhibit absorption peaks that are sufficiently similar or close enough to cause confusion when attempting glucose measurements *in vivo*.

To add further confusion, measurements can show a wide variation. This is especially so in ill persons when accurate and reliable blood glucose monitoring is most wanted. The blood glucose absorption peaks identified experimentally are often difficult to identify *in vivo*, being cluttered in amongst other peaks with a poor ratio of wanted signal to noise.

SUMMARY OF INVENTION

It is an object of the invention to provide a method and apparatus for monitoring blood sugar levels which reduces at least some of the problems associated with the prior art.

In one aspect the invention may be broadly said to consist in a method of measuring the level of sugar in blood *in vivo*, including the steps of:

(a) illuminating body tissue with near infrared light,

(b) detecting near infrared light returned from the illuminated tissue,

(c) determining the absorption, at at least one selected wavelength, of the near infrared light being returned, and

(d) deriving the level of sugar in the blood from the absorption determination,

wherein the blood is subject to a magnetic field to measurably alter the absorptive characteristics of the blood at the at least one selected near infrared wavelength and the body tissue is supplied with the blood after being subject to the magnetic field.

The body tissue may be part of a mammalian digit.

Preferably the body tissue is at the distal tip of the digit, and an intermediate portion of the digit is subjected to the magnetic field.

The magnetic field may be provided by at least one permanent magnet.

Alternatively, the magnetic field may be provided by at least one electromagnet.

The strength and/or polarity of the electromagnetic field may be changed in synchronism with the systolic and diastolic cycle of arterial blood supplied to said body tissue.

The measurement of the absorption of returned light may be synchronised with the systolic and diastolic cycle of arterial blood supplied to said body tissue.

Preferably, the systolic and diastolic cycle is determined by monitoring blood flows in said body tissue or in a closely related body part.

Preferably, the body tissue is part of a first mammalian digit and said systolic and diastolic cycle is determined by monitoring blood flows in a second digit on the same limb as said first digit.

The sugar may be blood glucose.

Preferably, the at least one selected wavelength is approximately 1586, 2122, 2272 or 2324 nm.

Preferably, the measurement is made non-invasively.

In another aspect the invention may be broadly said to consist in a device for making a non-invasive *in vivo* measurement of the level of sugar in blood at a sample zone, the device including a light source adapted for illuminating blood at the sample zone with near infrared light, a detector adapted for sensing near infrared light returned from said sample zone, and a magnet adapted for exerting a magnetic field on blood travelling to said sample

zone, the magnetic field being sufficient to measurably alter the absorption of light at at least one selected near infrared wavelength by the blood travelling to said sample zone.

The sample zone may be part of a mammalian digit.

Preferably the sample zone is at a tip portion of the digit and the magnet is adapted for exerting the magnetic field at an intermediate portion of the digit.

The device may include a blood oxygen monitor adapted for determining the systolic and diastolic cycle of arterial blood supplied to the sample zone, wherein operation of the light source is synchronised with the systolic and diastolic cycle.

Preferably the sample zone is a first digit and the blood oxygen monitor is adapted for monitoring the flow of blood in a second digit on the same limb as the first digit.

The magnet may include at least one permanent magnet.

The magnet may include at least one electromagnet.

Preferably the strength and/or polarity of the magnetic field is changed in synchronism with the systolic and diastolic cycle.

Preferably the near infrared light has a wavelength of approximately 1586, 2122, 2272 or 2324 nm.

The invention may further be said to consist in any alternative combination of parts or features mentioned herein or shown in the accompanying drawings. Known equivalents of these parts or features which are not expressly set out are nevertheless deemed to be included.

BRIEF DESCRIPTION OF DRAWINGS

Preferred forms, systems and methods of the invention will be further described with reference to the accompanying figures wherein;

Figure 1 shows a schematic view of a first apparatus for monitoring blood sugar levels, and

Figure 2 shows a schematic view of a second apparatus for monitoring blood sugar levels.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Referring to the drawings it will be appreciated that an apparatus for monitoring blood sugar levels according to the present invention may be implemented in various forms. The following embodiments are described by way of example only and are not intended to be limiting.

Figure 1 shows a side view of a distal end portion of a finger 1. The tip portion 2 of the finger is housed in a housing 3 which is shown in cross-section. The housing places a light source 4 and light detector 5 over the nail 6 of the finger. The light source is controlled by a controller 7.

A magnetic device 8 is positioned alongside an intermediate portion of the finger. The magnetic device may be one or more permanent magnets or electromagnets. The housing 3, light source 4, light detector 5 and controller 7 are shown schematically in Figure 1.

Figure 2 shows a plan view of a hand 10. The tip portion 11 of the index finger 12 is housed in a housing 13 which is shown in cross-section. The housing places a light source (not shown) and light detector (not shown) over the nail 14 of the index finger. An electromagnetic device 15 is positioned alongside an intermediate portion 16 of the finger. The light source and the magnetic device are controlled by respective controllers 17, 18.

An oximeter 19 is placed at the tip 20 of a second finger 21. A synchronisation trigger signal, derived from the oximeter by a signal processor 22 and synchronisation controller 23, is provided to the light source controller 17 and the magnetic device controller 18 to synchronise operation of the light source and magnetic device, as will be explained further below. The processor 22 and controllers 17, 18, 23 are shown schematically in Figure 2.

The light sources of the arrangements of Figures 1 and 2 are each a source of near infrared light, for example a light emitting semiconductor diode. References herein to 'light' are not intended to be limited to visible light but are to be understood as also including non-visible, and particularly near infrared (NIR), radiation or 'light'. References herein to near infrared or NIR light are to be understood as including light having a wavelength between about 750 and 3000 nm.

When, in each of the arrangements of Figures 1 and 2, the housing is fitted over a finger tip, the light source illuminates finger tissue. It is to be appreciated that the present invention has equal applicability to fingers and toes. Preferably the illumination is projected at subungual tissue under a finger or toe nail. The use of a user's nail as a 'window' for penetration of the illuminating light to the arteriole capillaries contained in the subungual tissue is advantageous. The penetration of light through the nail is relatively constant, unlike through the skin where movement of the user can cause variations. The nail also provides a firm and solid surface to support the light source and detector.

The light detector receives light returned from the illuminated site. This light includes light reflected by the nail and light diffusely reflected off the subungual tissue. Some wavelengths of the light reflected from the subungual tissue will be absorbed by various body and tissue components. In particular, certain NIR wavelengths are absorbed by blood glucose. The degree of absorption at these characteristic glucose wavelengths is used to determine the level of glucose present. The light returned to the detector will exhibit absorption peaks at these wavelengths, allowing a determination of the blood glucose levels to be calculated using measurements of the absorption peak levels. The accuracy and selectivity of the blood glucose measurements may be improved by measuring

characteristic glucose absorption peaks at two or more wavelengths while also measuring the returned light level at a third wavelength not absorbed by glucose, as a control.

The magnetic devices 8, 15 each provide a magnetic field which measurably alters the arterial blood flowing towards the illumination site at the tip 2, 11 of the respective finger 1, 12 by augmenting absorption peaks characteristic of glucose in the blood. *In vitro* experiments have shown increased NIR absorption after exposure of glucose to a magnetic field, and particularly in glucose absorption peaks at about 1586, 2122, 2272 and 2324 nm.

To reduce power requirements, particularly in a portable blood sugar monitoring device, the device advantageously uses a permanent magnetic device, and circuitry including the light source and detector, and an electromagnet if present, may also be switched on only momentarily to perform a measurement. Furthermore, the momentary switching on of the light source, by the light controller, also reduces the possibility of adverse effects on body tissue exposed to the NIR light.

In the arrangement of Figure 2, the electromagnet 15 and the light source are each controlled to synchronise the measurement of blood glucose with the user's systolic and diastolic cycle. This synchronisation optimises the measurement of blood glucose by taking the measurement at the point in the systolic and diastolic cycle when arterial blood is being delivered to the measurement site.

A pulse oximeter 19 is used to derive a synchronisation signal for controlling the emission of light by the light source at the height of the arterial pulsation, i.e. at the systolic phase of the cycle, when subungual capillaries at the nail bed are filled. The oximeter may be shaped as a cap or finger-glove for fitting over a finger of the user. The oximeter measures the level of oxygen in the blood at the bed of the nail by monitoring the absorption of light at a wavelength corresponding to an absorption peak of oxy-haemoglobin. The oximeter produces a signal having a waveform due the flow of blood in the capillaries at the finger tip. This waveform corresponds to the systolic and diastolic cycle of the arterial pulse.

The waveform from the oximeter is fed to a signal processor 22 and synchronisation controller 23. Although these are shown as discrete blocks, these functions may be provided by a common processor, for example a microprocessor, which can also process the detector signals and control other functions of the blood glucose monitor.

The synchronisation controller 23 synchronises the operation of the light source, by commencing illumination of the subungual region with NIR light when the waveform is rising at an upstroke through a threshold value, as at the systole, and ceasing illumination when the waveform passes back down through the threshold at the end of the peak. In this manner the light source emits NIR light at the peaks of the waveform generated by the oximeter, i.e. at the stystolic phase of the pulsation, when the capillaries receive arterial blood, when the signal to noise ratio of the glucose absorption component of returned light received by the detector is at the maximum achievable level. The synchronisation controller also activates the detector to measure the light returned from the illuminated subungual site at the same time. Measurements may be repeated over several cycles and averaged to further enhance the reliability of the measurements.

A baseline reading representing the blood sugar content of all body and tissue components at the illuminated site, except the arterial blood sugar, may also be made by taking a measurement between the peaks of the waveform generated by the oximeter. This baseline measurement, which may also be averaged over several cycles, may be used to provide a correction to the arterial blood glucose measurement.

As noted above, the synchronisation controller 23 synchronises the operation of the electromagnet 15 via the magnet controller 18. This is done to maximise the augmentation of the glucose absorption peaks by the magnetic field. The electromagnet is activated before the systolic peak. This is to allow time for the blood subjected to the magnetic field to move to the subungual region where, in synchronism with the systolic peak, it will be illuminated with NIR light and the returned light detected. The magnet controller 18 may control the strength and/or polarity of the magnetic field, and may synchronise these changes with the systolic and diastolic cycles, for example as derived from the oximeter. Control of the magnetic field strength may include switching the magnetic field on and off.

The devices and methods of the present invention provide for the measurement of blood glucose levels *in vivo*, i.e. in a living organism. Furthermore this can be achieved by the present invention non-invasively, i.e. without puncturing the skin or entering a body cavity.

5

The foregoing describes the invention including preferred forms thereof. Alterations and modifications as will be obvious to those skilled in the art are intended to be incorporated within the scope hereof as defined in the accompanying claims.

CLAIMS

Include reference numerals of features in the drawings

1 A method of measuring the level of sugar in blood *in vivo*, including the steps of:

(a) illuminating body tissue with near infrared light,

(b) detecting near infrared light returned from the illuminated tissue,

(c) determining the absorption, at at least one selected wavelength, of the near infrared light being returned, and

(d) deriving the level of sugar in the blood from the absorption determination,

wherein the blood is subject to a magnetic field to measurably alter the absorptive characteristics of the blood at the at least one selected near infrared wavelength and the body tissue is supplied with the blood after being subject to the magnetic field.

2 The method of measuring the level of sugar in blood as claimed in claim 1, wherein the body tissue is part of a mammalian digit.

3 The method of measuring the level of sugar in blood as claimed in claim 2, wherein the body tissue is at the distal tip of the digit, and an intermediate portion of the digit is subjected to the magnetic field.

4 The method of measuring the level of sugar in blood as claimed in any one of the preceding claims, wherein the magnetic field is provided by at least one permanent magnet.

5 The method of measuring the level of sugar in blood as claimed in any one of the preceding claims, wherein the magnetic field is provided by at least one electromagnet.

6 The method of measuring the level of sugar in blood as claimed in claim 5, wherein the strength of the electromagnetic field is changed in synchronism with the systolic and diastolic cycle of arterial blood supplied to said body tissue.

7 The method of measuring the level of sugar in blood as claimed in claim 5 or 6, wherein the polarity of the electromagnetic field is changed in synchronism with the systolic and diastolic cycle of arterial blood supplied to said body tissue.

8 The method of measuring the level of sugar in blood as claimed in any one of the preceding claims, wherein measurement of the absorption of returned light is synchronised with the systolic and diastolic cycle of arterial blood supplied to said body tissue.

9 The method of measuring the level of sugar in blood as claimed in any one of claims 6, 7 and 8, wherein said systolic and diastolic cycle is determined by monitoring blood flows in said body tissue or in a closely related body part.

10 The method of measuring the level of sugar in blood as claimed in claim 9, wherein said body tissue is part of a first mammalian digit and said systolic and diastolic cycle is determined by monitoring blood flows in a second digit on the same limb as said first digit.

11 The method of measuring the level of sugar in blood as claimed in any one of the preceding claims, wherein the sugar is blood glucose.

12 The method of measuring the level of sugar in blood as claimed in any one of the preceding claims, wherein the at least one selected wavelength is approximately 1586, 2122, 2272 or 2324 nm.

13 The method of measuring the level of sugar in blood as claimed in any one of the preceding claims, wherein the measurement is made non-invasively.

14 A device for making a non-invasive *in vivo* measurement of the level of sugar in blood at a sample zone, the device including a light source (4), adapted for illuminating blood at the sample zone with near infrared light, a detector (5) adapted for sensing near infrared light returned from said sample zone, and a magnet (8, 15) adapted for exerting a magnetic field on blood travelling to said sample zone, the magnetic field being sufficient

to measurably alter the absorption of light at at least one selected near infrared wavelength by the blood travelling to said sample zone.

15 A device as claimed in claim 14, wherein the sample zone is part of a mammalian digit (1, 12).

16 A device as claimed in claim 15, wherein the sample zone is at a tip portion (2, 11) of the digit and the magnet (8, 15) is adapted for exerting the magnetic field at an intermediate portion of the digit.

17 A device as claimed in claim 14, 15 or 16, including a blood oxygen monitor (19) adapted for determining the systolic and diastolic cycle of arterial blood supplied to the sample zone, wherein operation of the light source is synchronised with said systolic and diastolic cycle.

18 A device as claimed in claim 17, wherein the sample zone is a first digit (12) and the blood oxygen monitor is adapted for monitoring the flow of blood in a second digit (21) on the same limb as the first digit.

19 A device as claimed in any one of claims 14 to 18, wherein the magnet includes at least one permanent magnet.

20 A device as claimed in any one of claims 14 to 18, wherein the magnet includes at least one electromagnet.

21 A device as claimed in claim 20 when dependent upon claim 17 or 18, wherein the strength of the magnetic field is changed in synchronism with said systolic and diastolic cycle.

22 A device as claimed in claim 20 when dependent upon claim 17 or 18, wherein the polarity of the magnetic field is changed in synchronism with said systolic and diastolic cycle.

23 A device as claimed in any one of claims 14 to 22, wherein said near infrared light has a wavelength of approximately 1586, 2122, 2272 or 2324 nm.