DISPOSABLE GLUCOSE TEST STRIPS, AND METHODS AND COMPOSITIONS FOR MAKING SAME

BACKGROUND OF THE INVENTION

This application relates to disposable glucose test strips for use in electrochemical determinations of blood glucose, and to methods and compositions for use in making such strips.

Glucose monitoring is a fact of everyday life for diabetic individuals, and the accuracy of such monitoring can literally mean the difference between life and death. To accommodate a normal life style to the need for frequent monitoring of glucose levels, a number of glucose meters are now available which permit the individual to test the glucose level in a small amount of blood.

Many of these meters detect glucose in a blood sample electrochemically, by detecting the oxidation of blood glucose using an enzyme such as glucose oxidase provided as part of a disposable, single use electrode system. Examples of devices of this type are disclosed in European Patent No. 0 127 958, and U.S. Pat. Nos. 5,141,868, 5,286,362, 5,288,636, and 5,437,999 which are incorporated herein by reference.

In general, existing glucose test strips for use in electrochemical meters comprise a substrate, working and reference electrodes formed on the surface of the substrate, and a means for making connection between the electrodes and the meter. The working electrode is coated with an enzyme capable of oxidizing glucose, and a mediator compound which transfers electrons from the enzyme to the electrode resulting in a measurable current when glucose is present. Representative mediator compounds include ferricyanide, metallocene compounds such as ferrocene, quinones, phenazinium salts, redox indicator DCPIP, and imidazole-substituted osmium compounds.

Working electrodes of this type have been formulated in a number of ways. For example, mixtures of conductive carbon, glucose oxidase and a mediator have been formulated into a paste or ink and applied to a substrate. EP 0 127 958 and U.S. Pat. No. 5,286,362. In the case of disposable glucose strips, this application is done by screen printing in order to obtain the thin layers suitable for a small flat test strip. The use of screen printing, however, introduces problems to the operation of the electrode.

Unlike a thicker carbon paste electrode which remains fairly intact during the measurement, screen printed electrodes formed from carbon pastes or inks are prone to break up on contact with the sample. The consequences of this breakup are two-fold. Firstly, the components of the electrode formulation are released into solution. Once these components drift more than a diffusion length away from the underlying conductive layer, they no longer contribute toward the measurement, but in fact diminish the response by depleting inwardly-diffusing analyte. Secondly, the breakup of the screen printed electrode means that the effective electrode area is falling over time.

The combination of these two effects results in current transients which fall rapidly from an initial peak over the period of the measurement, and a high sensitivity to oxygen which quickly competes with the mediator for the enzyme. This fact is clearly demonstrated by the much lower currents measured in blood samples than in plasma samples or other aqueous media, and can result in erroneous readings. A further consequence is that the transients are often "lumpy" as the electrode breaks up in a chaotic manner. Lumpy transients either give rise to erroneous readings or rejected strips, neither of which are acceptable.

In addition to the potential for electrode breakup of screen-printed carbon-based electrodes, known electrodes used in disposable glucose test strips have been kinetically-controlled, i.e., the current depends on the rate of conversion of glucose by the enzyme. Because the response measured by the instrument represents a balance between the reaction of enzyme and mediator, enzyme and glucose and enzyme and oxygen, and because each of these reactions has its own dependence on temperature, the response of a kinetically-controlled test strip is very sensitive to the temperature of the sample. Substantial variation in the measured glucose value can therefore occur as a result of variations in sample handling.

Because of the importance of obtaining accurate glucose readings to the well-being of a patient using the meter and disposable test strips, it would be highly desirable to have a glucose test strip which did not suffer from these drawbacks, and which therefore provided a more consistent and reliable indication of actual blood glucose values, regardless of actual conditions. It is therefore an object of the present invention to provide disposable glucose test strips which are not prone to electrode breakup on contact with a sample.

It is a further object of this invention to provide glucose test strips which provide a glucose reading that is essentially independent of the hematocrit of the sample.

It is a further object of the present invention to provide glucose test strips which are substantially independent of temperature over a range between normal body temperature and room temperature.

It is a further object of the invention to provide test strips which provide a substantially flat current transient, without significant decay for periods of at least 10 seconds after the peak current level is obtained.

SUMMARY OF THE INVENTION

The present invention provides an improved disposable glucose test strip for use in a test meter of the type which receives a disposable test strip and a sample of blood from a patient and performs an electrochemical analysis of the amount of glucose in the sample. The test strip comprises:

(a) a substrate;

(b) a reference electrode;

(c) a working electrode; and

(d) means for making an electrical connection between the reference and working electrode and a glucose test meter. The working electrode comprises a conductive base layer disposed on the substrate and a non-conductive coating disposed over the conductive base layer. The non-conductive coating comprises a filler which has both hydrophobic and hydrophilic surface regions, an enzyme effective to oxidize glucose, e.g., glucose oxidase, and a mediator effective to transfer electrons from the enzyme to the conductive base layer. The filler is selected to have a balance of hydrophobicity and hydrophilicity such that on drying it forms a two-dimensional network on the surface of the conductive base layer. Preferred filler are non-conductive silica fillers. The response of this test strip is dependent on the diffusion rate of glucose, not on the rate at which the enzyme can oxidize glucose, such that the performance of the test strip is essentially temperature independent over relevant temperature ranges. Further, the silica appears to form a two-dimensional network