Given the ramifications of accurate recording, reporting and analyzing of blood ketone measurements in addition to blood glucose measurements, improvements in the techniques, procedures and equipment for testing blood ketone levels and/or blood ketone and blood glucose levels are desired.

Summary

Systems and methods for multiple analyte analysis are provided. In one aspect, there is provided a method, comprising: providing a test element configured for electrochemically analyzing first and second analytes in a sample, wherein the first analyte is a ketone and the second analyte is glucose; contacting the test element with the sample; determining concentration of the first analyte in the sample via a test meter configured to interact with the test element and providing an indication related to concentration of the first analyte in response to determining the first analyte concentration is above a predetermined value of at least 0.6 mM; determining concentration of the second analyte in the sample and automatically providing the concentration of the second; and determining concentration of the first analyte in the sampleinitiating a ketone watch if the second analyte concentration is above a predetermined value of at least about 240 mg/dL, wherein the ketone watch comprises at least one action selected from the group consisting of: (1) recommending increased frequency of testing for at least one of the first analyte and the second analyte, (2) automatically providing the concentration of the first analyte concentration with the concentration of the second analyte regardless of the value of the concentration of the second analyte, and (3) initiating a ketone trending analysis that monitors for rising first analyte concentration values, wherein each first analyte concentration is stored or retained regardless of whether each first analyte concentration is above the predetermined value of at least about 0.6 mM to permit trending analysis to be conducted on the stored or retained first analyte concentration values. In one embodiment, a method includes determining concentrations of first and second analytes in a sample. The first and second analytes may be, for example, glucose and a ketone such as hydroxybutryate. For reference in this application, the term "ketone" is understood to refer to and include ketone bodies such as hydroxybutyrate. In this form, an indication related to the measured concentration of hydroxybutyrate is provided in

response to determining that the concentration of hydroxybutyrate is above a predetermined value. In a further ~~aspect~~ embodiment of this form, a quantitative indication representative of the measured glucose concentration is automatically provided regardless of the value of the measured glucose concentration. In a yet further embodiment~~aspect~~, each measured concentration of hydroxybutyrate is stored or otherwise retained regardless of whether that measured concentration is above a predetermined value in order to permit trending analysis to be conducted with respect to all measured concentrations of hydroxybutyrate. ~~In another embodiment,~~ There is also provided a system includes a meter configured to interact with a test element to assess first and second analytes in a sample. In another aspect, there is provided a system, comprising: a test element configured for analyzing first and second analytes in a sample; and a meter configured to interact with the test element and including a controller structured to: determine concentration of the first analyte in the sample and, if the concentration of the first analyte is above a predetermined value, provide a first signal for providing an indication related thereto; and determine concentration of the second analyte in the sample and provide a second signal for outputting information related to the concentration of the second analyte. Other aspects and embodiments of the subject application are directed to unique techniques for analyzing analytes in a sample. Further embodiments, forms, objects, features, advantages, aspects, and benefits shall become apparent from the description and drawings.

In an additional embodiment, a method includes providing a test element configured for analyzing first and second analytes in a sample; contacting the test element with the sample; determining concentration of the first analyte in the sample and providing an indication in response to determining the first analyte concentration is above a predetermined

value; and determining concentration of the second analyte in the sample. In one form, the method further includes displaying information corresponding to the second analyte concentration. In another form, the first analyte is hydroxybutyrate and the second analyte is glucose. In still another form, the predetermined value is 0.6 mM. In another form, the step of providing the indication in response to determining the first analyte concentration is above a predetermined value includes at least one of displaying the first analyte concentration, providing a warning, providing a list of actions to take in response to the first analyte concentration being above the predetermined value, and transmitting a message to at least one of a user of the test element, healthcare provider, caregiver and parent or guardian.

In yet another form of this embodiment, providing the indication in response to determining the first analyte concentration is above the predetermined level includes transmitting a message to a mobile device or computer. In one ~~aspect~~ embodiment of this form, providing the indication in response to determining the first analyte concentration is above the predetermined level further includes displaying a message related to the first analyte concentration on a test meter. In another form, providing the indication in response to determining the first analyte concentration is above the predetermined level includes displaying a message related to the first analyte concentration. In one other form, providing the indication in response to determining the first analyte concentration is above the predetermined level includes changing a color or a shading of at least a portion of a display screen or textual display. In still another form, providing the indication in response to determining the first analyte concentration is above the predetermined level includes displaying an information icon on a display screen. In still another form, providing the indication in response to determining the first analyte concentration is above the predetermined level includes displaying an information icon on a display screen with an audio tone or vibration to encourage the patient to take notice. In one embodiment ~~aspect~~ of this form, the method further includes providing a message in response to a selection of the information icon. In a further embodiment~~aspect~~, the message includes at least one of a description of the first analyte concentration, a list of actions to take in response to the first analyte concentration being above the predetermined level, and contact information of a healthcare provider.

In another embodiment, a system includes a test element configured for analyzing first and second analytes in a sample. The system also includes a meter configured to interact with the test element and including a controller structured to: determine concentration of the first analyte in the sample and, if the concentration of the first analyte is above a predetermined value, provide a first signal for providing an indication related thereto; and determine concentration of the second analyte in the sample and provide a second signal for outputting information related to the concentration of the second analyte. In one form of this embodiment, the indication includes at least one of outputting information corresponding to the concentration of the first analyte, providing a warning, providing a list of actions to take in response to the first analyte concentration being above the predetermined value, and transmitting information related to the concentration of the first analyte to at least one of a user of the system, healthcare provider, caregiver and parent or guardian. In another form, the first analyte is hydroxybutyrate and the second analyte is glucose. In one embodiment ~~aspect~~ of this form, the predetermined value is in the range of 0.5 mM to 3.0 mM.

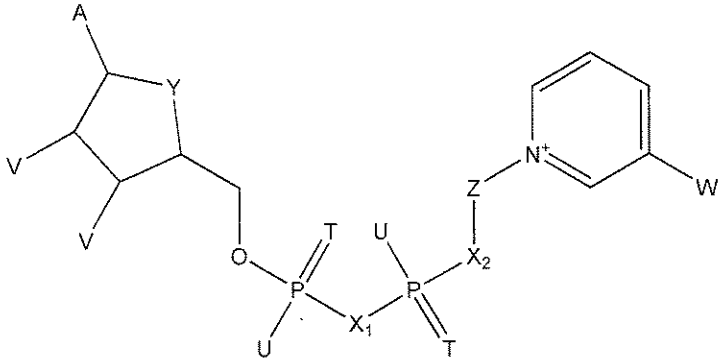
In another form of this embodiment, the meter further includes a display responsive to the first signal to display the indication related to the concentration of the first analyte. In one embodiment ~~aspect~~ of this form, the display is responsive to the first signal to provide an icon related to the concentration of the first analyte. In another embodiment ~~aspect~~ of this form, at least a portion of the display is configured to change color or shading in response to the first signal. In yet another embodiment ~~aspect~~ of this form, the display is configured to provide an information icon in response to the first signal. In a further embodiment~~aspect~~, the display is further configured to provide a message in response to a selection of the information icon, the message including at least one of a description of the first analyte concentration, a list of actions to take in response to the first analyte concentration being above the predetermined level, and contact information of a healthcare provider. In still another form of this embodiment, the meter further includes a communication module configured to transmit a message to a mobile device or computer in response to the first signal. In yet another form, the controller is further structured to provide a third signal for providing an approval indication if the concentration of the first analyte is below the predetermined value.

In a further embodiment, a method includes performing a plurality of tests to determine concentrations of first and second analytes in a sample. Each of the tests includes applying the sample to a test element configured for analyzing the first and second analytes in the sample. The method also includes storing the first analyte concentration determined from each test performed; analyzing the stored concentrations of the first analyte to monitor for an existence of any trends in the stored concentrations, such as toward a predetermined value or upwardly increasing over time, or as between common time periods such as specific time of day, weekend trends, or after specific events like meals, exercise or illness, and any interesting rate-of-change trends suggesting concerning changes in ketone/hydroxybutyrate levels regardless of whether any such levels are measured to be above a predetermined value; and providing a first indication in response to detecting the existence of the trend. The rate-of-change value to trigger a trend can be a preselected value or one that can be set by a person with diabetes or health care providers within reasonable ranges. In one form, the method also includes providing a second indication in response to determining the first analyte concentration is above the predetermined value in any one or more of the plurality of tests. In one embodiment ~~aspect~~ of this form, the method further includes automatically providing a third indication related to the concentration of the second analyte after performing each of the tests. In a further embodiment~~aspect~~, the first analyte is hydroxybutyrate and the second analyte is glucose.

In another form of this embodiment, the first indication includes one of a graphical illustration of the trend and an information icon. In still another form, providing the first indication includes displaying an information icon on a meter display. In another form, the method further includes providing a graphical illustration of the trend in response to a selection of the information icon. In another form of this embodiment, a graphical illustration of a trend is shown automatically if the trend meets some pre-specified criteria. Such criteria could be for example: one or more measured values coming close to or exceeding a pre-specified hydroxybutyrate value, the max/min hydroxybutyrate level over the past days/weeks/months is greater than a pre-specified value, or other criteria such as initiation of a "ketone watch" or measured values trending toward initiation of a "ketone watch".

when the trending information generally matches the predetermined criteria. In one embodiment ~~aspect~~ of this form, the first analyte is hydroxybutyrate and the second analyte is glucose, and the analyte selected for monitoring comprises hydroxybutyrate.

In another form of this embodiment, the watch mode comprises the device providing at least one recommendation for an increased frequency for determining the concentration for at least one of the first and second analytes. In yet another form, the method further includes, when the watch mode is activated, displaying a visual indication on the display, the visual indication configured to indicate the activation of the watch mode. In another form of this method, the first analyte is hydroxybutyrate and the second analyte is glucose.In one non-limiting form, one or more of the embodiments described above may involve a test element that includes a first coenzyme-dependent enzyme or a substrate for the first enzyme and a second coenzyme-dependent enzyme or a substrate for the second enzyme. The test element also includes a coenzyme selected from the group consisting of thio-NAD, thio-NADP, and a compound according to formula (I):



(I)

in which

A = adenine or an analog thereof,

T = in each case independently denotes O or S,

U = in each case independently denotes OH, SH, BH_3^-, or $BCNH_2^-$,

V = in each case independently denotes OH or a phosphate group,

W = COOR, $CON(R)_2$, COR, or $CSN(R)_2$ in which R in each case independently denotes H or C_1-C_2-alkyl,

X_1, X_2 = in each case independently denote O, CH_2, $CHCH_3$, $C(CH_3)_2$, NH, or NCH_3,

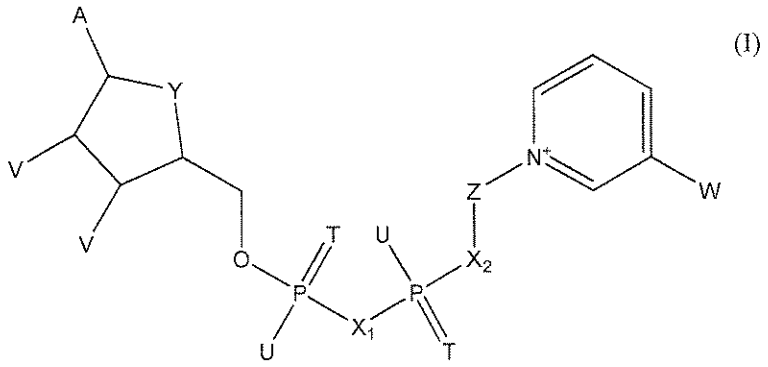
Y = NH, S, O, or CH_2,

Z = a residue comprising a cyclic group with 5 C atoms which optionally contains a heteroatom selected from O, S and N and optionally one or more substituents, and a residue $CR4_2$ wherein $CR4_2$ is bound to the cyclic group and to X_2, and

where R4 = in each case independently denotes H, F, Cl, or CH_3, provided that Z and the pyridine residue are not linked by a glycosidic bond,

or a salt or optionally a reduced form thereof.

In one embodiment~~aspect~~, the first analyte is hydroxybutyrate and the first enzyme is a hydroxybutyrate dehydrogenase. In a further embodiment~~aspect~~, the hydroxybutyrate dehydrogenase is 3-hydroxybutyrate dehydrogenase. In a further embodiment~~aspect~~, the second enzyme is a dehydrogenase selected from the group consisting of glucose dehydrogenase, lactate dehydrogenase, malate dehydrogenase, glycerol dehydrogenase, alcohol dehydrogenase, sorbitol dehydrogenase, and an amino acid dehydrogenase comprising L-amino acid dehydrogenase. In still another embodiment~~aspect~~, the second analyte is glucose and the second enzyme is a glucose dehydrogenase or a glucose oxidase. In a further embodiment~~aspect~~, the coenzyme is a compound according to formula (I)



(I)

in which

A = adenine,

T = in each case denotes O,

U = in each case denotes OH,

V = in each case denotes OH,

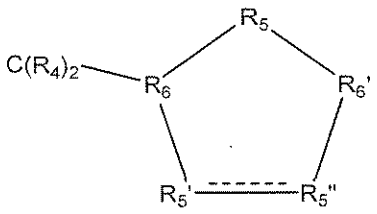
W = $CON(R)_2$ in which R denotes H,

X_1 = O,

X_2 = O,

Y = O, and

Z = a carbocyclic 5-membered ring of the general formula (II)



(II)

in which a single bond is present between R5' and R5", and in which

R4 = H,

R5' = CHOH,

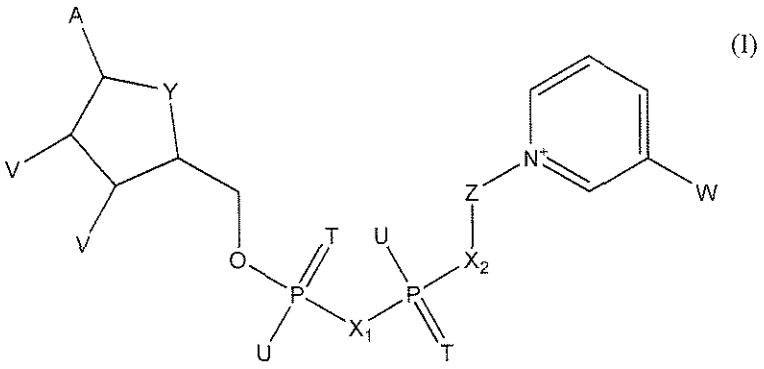
R5" = CHOH,

R5 = $CR4_2$,

R6 = CH, and

R6' = CH.

In yet another further embodiment~~aspect~~, the coenzyme is a compound according to formula (I)



(I)

in which

A = adenine,

T = in each case denotes O,

U = in each case denotes OH,

V = in a first case denotes OH and in a second case denotes a phosphate group,

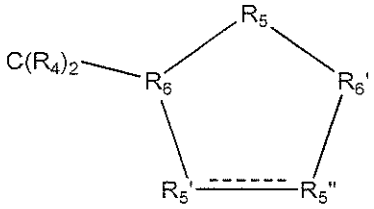
W = $CON(R)_2$ in which R denotes H,

X_1 = O,

X_2 = O,

Y = O, and

Z = a carbocyclic 5-membered ring of the general formula (II)



(II)

in which a single bond is present between R5' and R5", and in which

R4 = H,

R5' = CHOH,

R5" = CHOH,

$R5 = CR4_2$,

R6 = CH, and

R6' = CH.

In still another further embodimentaspect, the coenzyme is thio-NAD. In another further embodimentaspect, the coenzyme is thio-NADP.

In a further embodimentaspect, the test element includes a first reagent material which includes the first enzyme or the substrate for the first enzyme, and the coenzyme selected from the group consisting of thio-NAD, thio-NADP and the compound according to formula (I) or a salt or optionally a reduced form thereof. In a further embodimentaspect, the test element also includes a second reagent material which includes the second enzyme or the substrate for the second enzyme, and a coenzyme selected from the group consisting of FAD, NAD, NADP and the compound according to formula (I) or a salt or optionally a reduced form thereof. In a further embodimentaspect, the test element includes a test strip configured to carry the first and second reagent

materials. In yet another further embodiment~~aspect~~, the test strip includes a first electrode system associated with the first reagent material and a second electrode system associated with the second reagent material. In another embodiment~~aspect~~, the first reagent material further includes an electrochemical mediator or mediator precursor such as one of nitrosoaniline, potassium ferricyanide, a phenazine derivative, or hexaammineruthenium chloride or a combination thereof.

Further, although the description hereof discloses the use of a convenient dual test of ketone and glucose, persons of skill in the art will appreciate that other multi-analyte test strips may also be beneficial as a dual test with glucose and analytes such as 1,5 anhydroglucitol or HbA1c.

Another embodiment ~~aspect~~ of the present application is a unique technique for measuring the presence and/or concentration of multiple analytes in test samples. Other aspects and embodiments include unique methods, systems, devices, kits, assemblies, equipment, and/or apparatus related to analyte detection in a sample.

Further aspects, embodiments, forms, features, benefits, objects, and advantages shall become apparent from the detailed description and figures provided herewith.

Claims:

1. A method, comprising:

providing a test element configured for electrochemically analyzing first and second analytes in a sample, wherein the first analyte is a ketone and the second analyte is glucose;

contacting the test element with the sample;

determining concentration of the first analyte in the sample via a test meter configured to interact with the test element and providing an indication related to concentration of the first analyte in response to determining the first analyte concentration is above a predetermined value of at least 0.6 mM;

determining concentration of the second analyte in the sample and automatically providing the concentration of the second analyte; and

~~determining concentration of the first analyte in the sample~~initiating a ketone watch if the second analyte concentration is above a predetermined value of at least about 240 mg/dL, wherein the ketone watch comprises at least one action selected from the group consisting of:

(1) recommending increased frequency of testing for at least one of the first analyte and the second analyte,

(2) automatically providing the concentration of the first analyte concentration with the concentration of the second analyte regardless of the value of the concentration of the second analyte, and

(3) initiating a ketone trending analysis that monitors for rising first analyte concentration values, wherein each first analyte concentration is stored or retained regardless of whether each first analyte concentration is above the predetermined value of at least about 0.6 mM to permit trending analysis to be conducted on the stored or retained first analyte concentration values.

~~2. The method of claim 1, which further comprises:~~

~~providing an indication related to concentration of the first analyte in response to determining the first analyte concentration is above a predetermined value.~~

~~3. The method of claim 1 or 2, which further comprises displaying information corresponding to the second analyte concentration.~~

42. The method of ~~any of the preceding~~ claims 1, wherein the ketone ~~first analyte~~ is hydroxybutyrate ~~and the second analyte is glucose~~.

~~5. The method of any of the preceding claims , wherein the predetermined value is 0.6 mM.~~

63. The method of ~~any of the preceding~~ claims 1 or 2, wherein the step of providing the indication in response to determining the first analyte concentration is above a predetermined value includes at least one of displaying the first analyte concentration, providing a warning, providing a list of actions to take in response to the first analyte concentration being above the predetermined value, and transmitting a message to at least one of a user of the test element, healthcare provider, caregiver and parent or guardian.

~~7~~4. The method of any of the preceding claims~~-~~, wherein providing the indication in response to determining the first analyte concentration is above the predetermined level includes transmitting a message to a mobile device or computer.

~~8. The method of any of the preceding claims, wherein providing the indication in response to determining the first analyte concentration is above the predetermined level further includes displaying a message related to the first analyte concentration on a test meter.~~

~~9~~5. The method of any of the preceding claims~~-~~, wherein providing the indication in response to determining the first analyte concentration is above the predetermined level includes displaying a message related to the first analyte concentration.

~~10~~6. The method of any of the preceding claims~~-~~, wherein providing the indication in response to determining the first analyte concentration is above the predetermined level includes changing a color of at least a portion of a display screen of the test meter.

~~11~~7. The method of any of the preceding claims~~-~~, wherein providing the indication in response to determining the first analyte concentration is above the predetermined level includes displaying an information icon on a display screen of the test meter.

~~12~~8. The method of ~~any of the preceding~~ claims 7, which further includes providing a message in response to a selection of the information icon.

~~13~~9. The method of any of the preceding claims~~-~~, wherein the message includes at least one of a description of the first analyte concentration, a list of actions to take in response to the first analyte concentration being above the predetermined level, and contact information of a healthcare provider.

~~14~~10. A system, comprising:

a test element configured for analyzing first and second analytes in a sample; and

a meter configured to interact with the test element and including a controller structured to:

determine concentration of the first analyte in the sample and, if the concentration of the first analyte is above a predetermined value, provide a first signal for providing an indication related thereto; and

determine concentration of the second analyte in the sample and provide a second signal for outputting information related to the concentration of the second analyte.

~~15~~11. The system of claim ~~14~~10, wherein the indication includes at least one of outputting information corresponding to the concentration of the first analyte, providing a warning, providing a list of actions to take in response to the first analyte concentration being above the predetermined value, and transmitting information related to the concentration of the first analyte to at least one of a user of the system, healthcare provider, caregiver and parent or guardian.

~~16~~12. The system of any of the claims ~~14~~10 to ~~15~~11, wherein the first analyte is hydroxybutyrate and the second analyte is glucose.

~~17~~13. The system of any of the claims ~~14~~10 to ~~16~~12, wherein the predetermined value is in the range of 0.5 mM to 3.0 mM.

~~18~~14. The system of any of the claims ~~14~~10 to ~~17~~13, wherein the meter further includes a display responsive to the first signal to display the indication related to the concentration of the first analyte.

~~19~~15. The system of any of the claims ~~14~~10 to ~~18~~14, wherein the display is responsive to the first signal to provide an icon related to the concentration of the first analyte.

~~20~~16. The system of any of the claims ~~14~~10 to ~~19~~15, wherein at least a portion of the display is configured to change color in response to the first signal.

~~21~~17. The system of any of the claims ~~14~~10 to ~~20~~16, wherein the display is configured to provide an information icon in response to the first signal.

~~22~~18. The system of any of the claims ~~14~~10 to ~~21~~17, wherein the display is further configured to provide a message in response to a selection of the information icon, the message including at least one of a description of the first analyte concentration, a list of actions to take in response to the first analyte concentration being above the predetermined level, and contact information of a healthcare provider.

~~23~~19. The system of any of the claims ~~14~~10 to ~~21~~17, wherein the meter further includes a communication module configured to transmit a message to a mobile device or computer in response to the first signal.

~~24~~20. The system of any of the claims ~~14~~10 to ~~22~~18, wherein the controller is further structured to provide a third signal for providing an approval indication if the concentration of the first analyte is below the predetermined value.

~~25~~21. The method of claim 1 further comprising:

performing a plurality of tests to determine concentrations of first and second analytes in a sample, wherein each of the tests includes applying the sample to the test element configured for analyzing the first and second analytes in the sample;

storing the first analyte concentration determined from each test performed;

analyzing the stored concentrations of the first analyte to monitor for an existence of an upwardly increasing trend in the stored concentrations toward a predetermined value; and

providing a first indication in response to detecting the existence of the trend.

~~26~~22. The method of claim ~~25~~21, which further includes providing a second indication in response to determining the first analyte concentration is above the predetermined value in any one or more of the plurality of tests.

~~27~~23. The method of claim ~~25~~ 21 or ~~26~~22, which further includes automatically providing a third indication related to the concentration of the second analyte after performing each of the tests.

~~28~~24. The method of any of claims ~~25~~ 21 to ~~27~~23, wherein the first analyte is hydroxybutyrate and the second analyte is glucose.

~~29~~25. The method of any of claims ~~25~~ 21 to ~~28~~24, wherein the first indication includes one of a graphical illustration of the trend and an information icon.

~~30~~26. The method of any of claims ~~25~~ 21 to ~~29~~25, wherein providing the first indication includes displaying an information icon on a meter display.

~~31~~27. The method of any of claims ~~25~~ 21 to ~~30~~26, which further includes providing a graphical illustration of the trend in response to a selection of the information icon.

~~32~~28. The method of any of ~~the preceding~~ claims 1 to 9 and 21 to 27, further, comprising:

providing a hand held device comprising a display, a processor and a storage memory, the device being operative to engage one or more test elements and to determine concentration of at least first and second analytes in a fluid sample provided on said one or more test elements;

using the device, recording in the storage memory the value of the determined concentration of each of the at least first and second analytes;

using the device, determining whether the determined concentration for the first analyte is above a first predetermined value;

using the device, determining whether the determined concentration for the second analyte is above a second predetermined value; and

using the device, activating a watch mode when the determined concentration for either of the first and second analytes is above the respective first and second predetermined values.

~~33~~29. The method of claim ~~32~~28, wherein the storage memory comprises a plurality of recorded values of determined concentrations for each of the first and second analytes, the method further comprising:

selecting at least one of the first and second analytes for monitoring trending information;

using the device, determining whether the trending information for the analyte selected for monitoring generally matches predetermined criteria for recommending an increased frequency for determining the concentration for the analyte selected; and

using the device, activating the watch mode regardless of the determined concentration for either of the first and second analytes being above the respective first and second predetermined values when the trending information generally matches the predetermined criteria.

~~34~~30. The method of claim ~~32~~28 or ~~33~~29 wherein the first analyte is hydroxybutyrate and the second analyte is glucose, and the analyte selected for monitoring comprises hydroxybutyrate.

~~35~~31. The method of any of claims ~~32~~28 to ~~35~~30, wherein the watch mode comprises the device providing at least one recommendation for an increased frequency for determining the concentration for at least one of the first and second analytes.

~~36~~32. The method of any of claims ~~33~~ 29 to ~~35~~31, further comprising when the watch mode is activated, displaying a visual indication on the display, the visual indication configured to indicate the activation of the watch mode.

~~37~~33. The method of any of claims ~~32~~ 28 to ~~36~~32, wherein the first analyte is hydroxybutyrate and the second analyte is glucose.