SUMMARY

The purpose and advantages of the disclosed subject matter will be set forth in and apparent from the description that follows, as well as will be learned by practice of the disclosed subject matter. Additional advantages of the disclosed subject matter will be realized and attained by the methods and systems particularly pointed out in the written description and claims hereof, as well as from the appended drawings.

In one aspect, there is provided a method for inspecting a liquid beneficial agent contained within a container, comprising:

selectively illuminating at least a portion of the liquid beneficial agent;

obtaining an image from the illuminated portion of the liquid beneficial agent;

analyzing image data representing the image, using a data processor, to obtain a particle concentration;

measuring an image intensity value of the image data using the data processor;

determining a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value; and

rejecting the liquid beneficial agent if the quality level is below a predetermined threshold.

In one aspect, there is provided a system for inspecting a liquid beneficial agent within a container, comprising:

a light source configured to illuminate at least a portion of the liquid beneficial agent;

an image detector configured to obtain an image from the illuminated portion of the liquid beneficial agent; and

a data processor coupled to the image detector and programmed to:

analyze image data representing the image from the image detector to obtain a particle concentration,

measure an image intensity value of the image data,

determine a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value, and

reject the liquid beneficial agent if the quality level is below a predetermined threshold.

In one aspect, there is provided a beneficial treatment product, comprising:

a container containing a liquid beneficial agent;

a light source configured to illuminate at least a portion of the liquid beneficial agent;

an image detector configured to obtain an image from the illuminated portion of the liquid beneficial agent; and

a data processor coupled to the image detector and programmed to:

analyze image data representing the image from the image detector to obtain a particle concentration,

measure an image intensity value of the image data,

determine a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value, and

reject the liquid beneficial agent if the quality level is below a predetermined threshold.

In one aspect, there is provided a liquid beneficial agent having a predetermined quality level determined by the method as disclosed herein.To achieve these and other advantages and in accordance with the purpose of the disclosed subject matter, as embodied and broadly described, the disclosed subject matter includes a method for detection of particles in a liquid beneficial agent contained within a container. The method includes selectively illuminating at least a portion of the liquid beneficial agent; obtaining an image from the illuminated portion of the liquid beneficial agent; analyzing image data representing the image, using a data processor, to obtain a particle concentration;

measuring an image intensity value of the image data using the data processor; and determining a quality level of the liquid beneficial agent using the data processor based on the particle concentration and the measured image intensity value.

For example and as embodied herein, selectively illuminating a portion of the liquid beneficial agent can include focusing light through an optical element corresponding to the container to provide an undistorted image from the illuminated portion of liquid beneficial agent. Selectively illuminating the portion of the liquid beneficial agent can also include forming a thin sheet of illumination in the illuminated portion of the liquid beneficial agent. The liquid beneficial agent can be selectively illuminated with light having a wavelength in a range from about 200 nm to about 1100 nm.

In some embodiments, the image is obtained by or as a result of light scattering from the particles in the illuminated portion of the beneficial agent. Additionally or alternatively, the liquid beneficial agent can have intrinsic fluorescence, and the liquid beneficial agent can be selectively illuminated with light having an excitation wavelength suitable to cause the liquid beneficial agent to emit fluorescent light of an emission wavelength. Obtaining the image therefore can include using an optical filter corresponding to the emission wavelength of the emitted fluorescent light. Obtaining the image can also include focusing an image

SUMMARY

The purpose and advantages of the disclosed subject matter will be set forth in and apparent from the description that follows, as well as will be learned by practice of the disclosed subject matter. Additional advantages of the disclosed subject matter will be realized and attained by the methods and systems particularly pointed out in the written description and claims hereof, as well as from the appended drawings.

In one aspect, there is provided a method for inspecting a liquid beneficial agent contained within a container, comprising:

selectively illuminating at least a portion of the liquid beneficial agent;

obtaining an image from the illuminated portion of the liquid beneficial agent;

analyzing image data representing the image, using a data processor, to obtain a particle concentration;

measuring an image intensity value of the image data using the data processor by determining a pixel intensity value of each pixel of a plurality of pixels of the image data, and combining the pixel intensity values of the plurality of pixels to determine the image intensity value;

determining a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value; and

rejecting the liquid beneficial agent if the quality level is below a predetermined threshold.

In one aspect, there is provided a system for inspecting a liquid beneficial agent within a container, comprising:

a light source configured to illuminate at least a portion of the liquid beneficial agent;

an image detector configured to obtain an image from the illuminated portion of the liquid beneficial agent; and

a data processor coupled to the image detector and programmed to:

analyze image data representing the image from the image detector to obtain a particle concentration,

measure an image intensity value of the image data, by determining a pixel intensity value of each pixel of a plurality of pixels of the image data, and combining the pixel intensity values of the plurality of pixels to determine the image intensity value,

determine a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value, and

reject the liquid beneficial agent if the quality level is below a predetermined threshold.

In one aspect, there is provided a beneficial treatment product, comprising:

a container containing a liquid beneficial agent;

a light source configured to illuminate at least a portion of the liquid beneficial agent;

an image detector configured to obtain an image from the illuminated portion of the liquid beneficial agent; and

a data processor coupled to the image detector and programmed to:

analyze image data representing the image from the image detector to obtain a particle concentration,

measure an image intensity value of the image data, by determining a pixel intensity value of each pixel of a plurality of pixels of the image data, and combining the pixel intensity values of the plurality of pixels to determine the image intensity value,

determine a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value, and

reject the liquid beneficial agent if the quality level is below a predetermined threshold.

In one aspect, there is provided a liquid beneficial agent having a predetermined quality level determined by the method as described herein.

To achieve these and other advantages and in accordance with the purpose of the disclosed subject matter, as embodied and broadly described, the disclosed subject matter includes a method for detection of particles in a liquid beneficial agent contained within a container. The method includes selectively illuminating at least a portion of the liquid beneficial agent; obtaining an image from the illuminated portion of the liquid beneficial agent; analyzing image data representing the image, using a data processor, to obtain a particle concentration;

measuring an image intensity value of the image data using the data processor; and determining a quality level of the liquid beneficial agent using the data processor based on the particle concentration and the measured image intensity value.

For example and as embodied herein, selectively illuminating a portion of the liquid beneficial agent can include focusing light through an optical element corresponding to the container to provide an undistorted image from the illuminated portion of liquid beneficial agent. Selectively illuminating the portion of the liquid beneficial agent can also include forming a thin sheet of illumination in the illuminated portion of the liquid beneficial agent. The liquid beneficial agent can be selectively illuminated with light having a wavelength in a range from about 200 nm to about 1100 nm.

In some embodiments, the image is obtained by or as a result of light scattering from the particles in the illuminated portion of the beneficial agent. Additionally or alternatively, the liquid beneficial agent can have intrinsic fluorescence, and the liquid beneficial agent can be selectively illuminated with light having an excitation wavelength suitable to cause the liquid beneficial agent to emit fluorescent light of an emission wavelength. Obtaining the image therefore can include using an optical filter corresponding to the emission wavelength of the emitted fluorescent light. Obtaining the image can also include focusing an image

CLAIMS

1. A method for inspecting a liquid beneficial agent contained within a container, comprising:

selectively illuminating at least a portion of the liquid beneficial agent;

obtaining an image from the illuminated portion of the liquid beneficial agent;

analyzing image data representing the image, using a data processor, to obtain a particle concentration;

measuring an image intensity value of the image data using the data processor;

determining a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value; and

rejecting the liquid beneficial agent if the quality level is below a predetermined threshold.

2. The method according to claim 1, wherein selectively illuminating the portion of the liquid beneficial agent comprises focusing light through an optical element having a curvature corresponding to a curvature of the container to provide an undistorted image of the liquid beneficial agent.

3. The method according to claim 1, wherein selectively illuminating the portion of the liquid beneficial agent comprises forming a thin sheet of illumination in the illuminated portion of the liquid beneficial agent.

4. The method according to claim 1, wherein the liquid beneficial agent is selectively illuminated with light having a wavelength in a range from about 200 nm to about 1100 nm.

5. The method according to claim 1, wherein the image is obtained by light scattering from particles in the illuminated portion of the liquid beneficial agent.

6. The method according to claim 1, wherein the liquid beneficial agent has intrinsic fluorescence and the beneficial agent is selectively illuminated with light having an excitation wavelength suitable to cause the liquid beneficial agent to emit fluorescent light of an emission wavelength.

7. The method according to claim 6, wherein obtaining the image comprises using an optical filter corresponding to the emission wavelength of the emitted fluorescent light.

8. The method according to claim 1, wherein obtaining the image comprises focusing an image detector through an optical element corresponding to the container to provide an undistorted image from the liquid beneficial agent.

9. The method according to claim 1, wherein obtaining the image comprises:

capturing a first image and a second image from the illuminated portion of the liquid beneficial agent; and

using difference image analysis on the first image and the second image to obtain the image.

10. The method according to claim 1, further comprising calibrating an image detector to a predetermined sensitivity.

11. The method according to claim 1, wherein analyzing the image data to obtain a particle concentration threshold is performed using a single image frame.

12. The method of claim 1, wherein obtaining the particle concentration comprises counting a number of particles exceeding a size threshold to generate a particle size distribution.

13. The method of claim 12, wherein counting a number of particles exceeding a size threshold comprises measuring particle scattering intensities to estimate the particle size distribution.

14. The method according to claim 1, wherein measuring the image intensity value of the image data comprises:

determining a pixel intensity value of each pixel of a plurality of pixels of the image data using the data processor; and

combining the pixel intensity values of the plurality of pixels to determine the image intensity value using the data processor.

15. The method according to claim 1, wherein determining the quality of the liquid beneficial agent comprises comparing the particle concentration to a particle concentration threshold.

16. The method according to claim 15, wherein determining the quality of the liquid beneficial agent further comprises comparing the image intensity value to an image intensity threshold.

17. The method according to claim 16, wherein the particle concentration threshold and the image intensity threshold are obtained from a representative profile.

18. The method according to claim 1, further comprising determining an average molecular mass of the particles using the image intensity value, wherein the quality level is further determined using the average molecular mass.

19. The method according to claim 1, further comprising providing an indication to a user that the liquid beneficial agent is unsuitable if the quality level does not exceed a predetermined quality level.

20. The method according to claim 1, wherein the detection is performed on a plurality of containers in a high-throughput manner.

21. A system for inspecting a liquid beneficial agent within a container, comprising:

a light source configured to illuminate at least a portion of the liquid beneficial agent;

an image detector configured to obtain an image from the illuminated portion of the liquid beneficial agent; and

a data processor coupled to the image detector and programmed to:

analyze image data representing the image from the image detector to obtain a particle concentration,

measure an image intensity value of the image data,

determine a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value, and

reject the liquid beneficial agent if the quality level is below a predetermined threshold.

22. A beneficial treatment product, comprising:

a container containing a liquid beneficial agent;

a light source configured to illuminate at least a portion of the liquid beneficial agent;

an image detector configured to obtain an image from the illuminated portion of the liquid beneficial agent; and

a data processor coupled to the image detector and programmed to:

analyze image data representing the image from the image detector to obtain a particle concentration,

measure an image intensity value of the image data,

determine a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value, and

reject the liquid beneficial agent if the quality level is below a predetermined threshold.

23. A liquid beneficial agent having a predetermined quality level determined by the method of claim 1.

24. The liquid beneficial agent of claim 23, wherein the liquid beneficial agent comprises a small molecule.

25. The liquid beneficial agent of claim 23, wherein the liquid beneficial agent comprises a protein.

26. The liquid beneficial agent of claim 25, wherein the liquid beneficial agent has a protein concentration between about 0.1 mg/ml and about 200 mg/ml.

27. The liquid beneficial agent of claim 25, wherein the protein is a fusion protein.

28. The liquid beneficial agent of claim 25, wherein the protein is an antibody.

29. The liquid beneficial agent of claim 28, wherein the antibody is an anti-Tumor Necrosis Factor alpha (TNFα) antibody, or antigen-binding fragment thereof.

30. The method according to claim 18, wherein the average molecular mass is further determined using a background image intensity value.

31. The method according to claim 18, wherein the predetermined threshold of the quality level is a predetermined average molecular mass.

CLAIMS

1. A method for inspecting a liquid beneficial agent contained within a container, comprising:

selectively illuminating at least a portion of the liquid beneficial agent;

obtaining an image from the illuminated portion of the liquid beneficial agent;

analyzing image data representing the image, using a data processor, to obtain a particle concentration;

measuring an image intensity value of the image data using the data processor by determining a pixel intensity value of each pixel of a plurality of pixels of the image data, and combining the pixel intensity values of the plurality of pixels to determine the image intensity value;

determining a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value; and

rejecting the liquid beneficial agent if the quality level is below a predetermined threshold.

2. The method according to claim 1, wherein selectively illuminating the portion of the liquid beneficial agent comprises focusing light through an optical element having a curvature corresponding to a curvature of the container to provide an undistorted image of the liquid beneficial agent.

3. The method according to claim 1, wherein selectively illuminating the portion of the liquid beneficial agent comprises forming a thin sheet of illumination in the illuminated portion of the liquid beneficial agent.

4. The method according to claim 1, wherein the liquid beneficial agent is selectively illuminated with light having a wavelength in a range from about 200 nm to about 1100 nm.

5. The method according to claim 1, wherein the image is obtained by light scattering from particles in the illuminated portion of the liquid beneficial agent.

6. The method according to claim 1, wherein the liquid beneficial agent has intrinsic fluorescence and the beneficial agent is selectively illuminated with light having an excitation wavelength suitable to cause the liquid beneficial agent to emit fluorescent light of an emission wavelength.

7. The method according to claim 6, wherein obtaining the image comprises using an optical filter corresponding to the emission wavelength of the emitted fluorescent light.

8. The method according to claim 1, wherein obtaining the image comprises focusing an image detector through an optical element corresponding to the container to provide an undistorted image from the liquid beneficial agent.

9. The method according to claim 1, wherein obtaining the image comprises:

capturing a first image and a second image from the illuminated portion of the liquid beneficial agent; and

using difference image analysis on the first image and the second image to obtain the image.

10. The method according to claim 1, further comprising calibrating an image detector to a predetermined sensitivity.

11. The method according to claim 1, wherein analyzing the image data to obtain a particle concentration threshold is performed using a single image frame.

12. The method of claim 1, wherein obtaining the particle concentration comprises counting a discrete number of particles in the image data exceeding a size threshold and a particle intensity threshold to generate a particle size distribution.

13. The method of claim 12, wherein counting a number of particles exceeding a size threshold comprises measuring particle scattering intensities to estimate the particle size distribution.

14. The method according to claim 1, wherein determining the quality of the liquid beneficial agent comprises comparing the particle concentration to a particle concentration threshold.

15. The method according to claim 14, wherein determining the quality of the liquid beneficial agent further comprises comparing the image intensity value to an image intensity threshold.

16. The method according to claim 15, wherein the particle concentration threshold and the image intensity threshold are obtained from a representative profile.

17. The method according to claim 1, further comprising determining an average molecular mass of aggregates of the particles using the image intensity value, wherein the quality level is based on the determined average molecular mass of the aggregates.

18. The method according to claim 1, further comprising providing an indication to a user that the liquid beneficial agent is unsuitable if the quality level does not exceed a predetermined quality level.

19. The method according to claim 1, wherein the detection is performed on a plurality of containers in a high-throughput manner.

20. A system for inspecting a liquid beneficial agent within a container, comprising:

a light source configured to illuminate at least a portion of the liquid beneficial agent;

an image detector configured to obtain an image from the illuminated portion of the liquid beneficial agent; and

a data processor coupled to the image detector and programmed to:

analyze image data representing the image from the image detector to obtain a particle concentration,

measure an image intensity value of the image data, by determining a pixel intensity value of each pixel of a plurality of pixels of the image data, and combining the pixel intensity values of the plurality of pixels to determine the image intensity value,

determine a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value, and

reject the liquid beneficial agent if the quality level is below a predetermined threshold.

21. A beneficial treatment product, comprising:

a container containing a liquid beneficial agent;

a light source configured to illuminate at least a portion of the liquid beneficial agent;

an image detector configured to obtain an image from the illuminated portion of the liquid beneficial agent; and

a data processor coupled to the image detector and programmed to:

analyze image data representing the image from the image detector to obtain a particle concentration,

measure an image intensity value of the image data, by determining a pixel intensity value of each pixel of a plurality of pixels of the image data, and combining the pixel intensity values of the plurality of pixels to determine the image intensity value,

determine a quality level of the liquid beneficial agent using the data processor based on both the particle concentration and the measured image intensity value, and

reject the liquid beneficial agent if the quality level is below a predetermined threshold.

22. A liquid beneficial agent having a predetermined quality level determined by the method of claim 1.

23. The liquid beneficial agent of claim 22, wherein the liquid beneficial agent comprises a small molecule.

24. The liquid beneficial agent of claim 22, wherein the liquid beneficial agent comprises a protein.

25. The liquid beneficial agent of claim 24, wherein the liquid beneficial agent has a protein concentration between about 0.1 mg/ml and about 200 mg/ml.

26. The liquid beneficial agent of claim 24, wherein the protein is a fusion protein.

27. The liquid beneficial agent of claim 24, wherein the protein is an antibody.

28. The liquid beneficial agent of claim 27, wherein the antibody is an anti-Tumor Necrosis Factor alpha (TNFα) antibody, or antigen-binding fragment thereof.

29. The method according to claim 17, wherein the average molecular mass is further determined using a background image intensity value.

30. The method according to claim 17, wherein the predetermined threshold of the quality level is a predetermined average molecular mass.

31. The method according to claim 17, wherein the average molecular mass is linearly proportional to the measured image intensity value and the particle concentration.

32. The method according to claim 1, wherein the particle concentration is obtained to directly identify particles in the image, and wherein the image intensity value is measured to indirectly analyze other particles not directly identified by obtaining the particle concentration.

33. The method according to claim 1, wherein the particle concentration is obtained for particles having a size of 100 nm or greater.

34. The method according to claim 1, wherein the image intensity value of the image data is measured to detect particles having a size of less than 100 nm.

35. The method according to claim 1, wherein the the particle concentration is obtained to directly identify particles having a size of 100 nm or greater and the image intensity value is measured to indirectly analyze particles having a size of less than 100 nm.