Claims

1. A method for optically measuring at least the stability and the aggregation of particles in a liquid sample, which is in a sample container, wherein the method comprises the following steps:

irradiating the sample with light of at least a first wavelength, to fluorescently excite the particles,

irradiating the sample with light of at least a second wavelength to examine the scattering of the particles,

measuring the fluorescence light emitted by the sample; and

measuring the extinction light at the second wavelength, wherein the irradiated light of the second wavelength runs through the sample container, is reflected back, runs again through the sample container in opposite direction and exits as extinction light,

wherein the stability is measured on the basis of the measured fluorescence light and the aggregation on the basis of the measured extinction light;

wherein the sample container is shifted during a measuring period relatively to the irradiated light of the first and/or second wavelength and/or to the detector and is driven back and forth several times; and

wherein a plurality of sample containers or a plurality of capillaries are scanned by said relative movement.

2. The method according to claim 1, wherein the fluorescence light and the extinction light are measured with a common optical system.

3. The method according to claim 1, wherein the irradiation of the sample

i) is not conducted simultaneously with the first and second wavelengths; or

ii) the irradiation with the second wavelength is conducted continuously, whereas the irradiation with the first wavelength is conducted intermittently.

4. The method according to claim 1, wherein the fluorescence light and the extinction light

are measured simultaneously.

5. The method according to claim 1, wherein

   i) the extinction light and the fluorescence light are measured by a common detector;

   ii) the extinction light is measured by a first detector and/or a second detector and fluorescence light of a first fluorescence wavelength is measured by the first detector and fluorescence light of a second fluorescence wavelength is measured by the second detector; or

   iii) the extinction light is measured by a first detector, fluorescence light of a first fluorescence wavelength is measured by a second detector and fluorescence light of a second fluorescence wavelength is measured by a third detector.

6. The method according to claim 1, wherein the sample container is a capillary.

7. The method according to claim 1, wherein the sample container is tempered, preferably rests on a tempering element and is tempered by a contact, wherein the tempering element further preferably reflects back the irradiated light of the second wavelength, again runs through the sample container in opposite direction and exits as extinction light.

8. The method according to claim 7, wherein the tempering element is made of a material

   i) which has little autofluorescence <1%, and/or

   ii) which has a high reflectivity > 30% in the wavelength range of the second wavelength.

9. The method according to claim 1, wherein at the surface of the tempering element at least one groove is configured, the sample container is arranged above the groove and the irradiated light of the second wavelength is reflected back from the bottom of the groove.

10. The method according to claim 9, wherein the groove has a width between 1-10 mm and a depth of more than half of the coherence length of the light of the second wavelength.

11. The method according to claim 1, wherein

i) a fluorescence value is determined by integrating the intensity of the fluorescence light via the shifting and/or

ii) an extinction value is determined by integrating the intensity of the extinction light via the shifting.

12. The method according to claim 1, wherein during a measuring period

i) in order to determine the thermal stability the temperature of the samples is changed, preferably increased;

ii) in order to determine chemical stability the concentration of denaturants in different liquid samples is chosen differently; and/or

iii) in order to determine stability in terms of time the sample is kept at a substantially constant temperature via a time period of more than one hour.

13. The method according to claim 1, wherein during a measuring period a plurality of sample containers and/or the optical system are continuously driven back and forth several times and the measurements of the fluorescence light and/or the extinction light are conducted during the movement.

14. The method according to claim 1, wherein the second wavelength is chosen such that less than 1%, 0.1%, 0.05% is absorbed by the sample or the particles in the sample.

15. The method according to claim 1, wherein the light of the first wavelength and the light of the second wavelength are united to a collinear ray which is irradiated into the sample container.

16. The method according to claim 1, wherein the extinction light of the second wavelength, which is reflected back and leaves the sample container in the opposite direction to the irradiation direction, deviates from the irradiation direction 5° at most.

17. An apparatus for the optical measurement of the stability and the aggregation of particles in a liquid sample, which is located in a sample container, in particular according to any one of the preceding claims, wherein the apparatus comprises:

a first light source for irradiating light of a first wavelength into the sample container to fluorescently excite the particles to be examined,

a second light source for irradiating light of a second wavelength into the sample container to measure the scattering of the particles,

a first detector for measuring the excited fluorescence light which is radiated from the sample,

a second detector for measuring extinction light at the second wavelength wherein the irradiated light of the second wavelength runs through the sample container, is reflected back, runs again through the sample container in the opposite direction and exits as extinction light; and

an evaluation means which determines the stability of the particles based on the measured fluorescence light and which determines the aggregation of the particles based on the measured extinction light;

wherein the sample container is configured to shift during a measuring period relative to the irradiated light of the first and/or second wavelength and/or to the detector and is configured to be driven back and forth several times; and

wherein a plurality of sample containers or a plurality of capillaries are configured to be scanned by said relative movement.

18. The apparatus according to claim 17 comprising a tempering element with a reflecting surface at which the irradiated light of the second wavelength is reflected back, and

wherein the apparatus is preferably configured to arrange at least one sample container on the surface for measurement purposes.

19. The apparatus according to claim 18, wherein the at least one sample container is a capillary.

20. The apparatus according to claim 18, wherein the reflective surface consists of silicon.

21. The apparatus according to claim 18, wherein at least one groove is configured at the surface of the tempering element, the sample container is arranged above the groove and the irradiated light of the second wavelength is reflected back from the bottom of the groove.

22. The apparatus according to claim 21, wherein the groove has a width between 1-10 mm and a depth of more than half of the coherence length of the light of the second wavelength.

23. The use of an apparatus according to claim 17 for conducting a method for optically measuring at least the stability and the aggregation of particles in the liquid sample, which is in the sample container, wherein the method comprises the following steps:

irradiating the sample with the light of at least the first wavelength, to fluorescently excite the particles,

irradiating the sample with the light of at least the second wavelength to examine the scattering of the particles,

measuring the fluorescence light emitted by the sample; and

measuring the extinction light at the second wavelength, wherein the irradiated light of the second wavelength runs through the sample container, is reflected back, runs again through the sample container in opposite direction and exits as extinction light,

wherein the stability is measured on the basis of the measured fluorescence light and the aggregation on the basis of the measured extinction light;

wherein the sample container is shifted during a measuring period relatively to the irradiated light of the first and/or second wavelength and/or to the detector and is driven back and forth several times; and

wherein the plurality of sample containers or the plurality of capillaries are scanned by said relative movement.