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(54) **SYRINGE**

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(57) **ABSTRACT**

Provided is a syringe with which it is possible to hold with greater stability a liquid inside the barrel while maintaining the slidability and air-tightness between the barrel and the gasket without requiring fixation of silicone oil, and which is excellent in terms of accuracy of visual inspection. The syringe has a resin barrel, a gasket slidably inserted inside the barrel, a plunger attached to the gasket, and a silicone film obtained by applying silicone oil having a kinematic viscosity of 500 to 10,000 cSt over the inner peripheral surface of the barrel in an amount of 5 to 50 μg per 1 cm^2 of area.

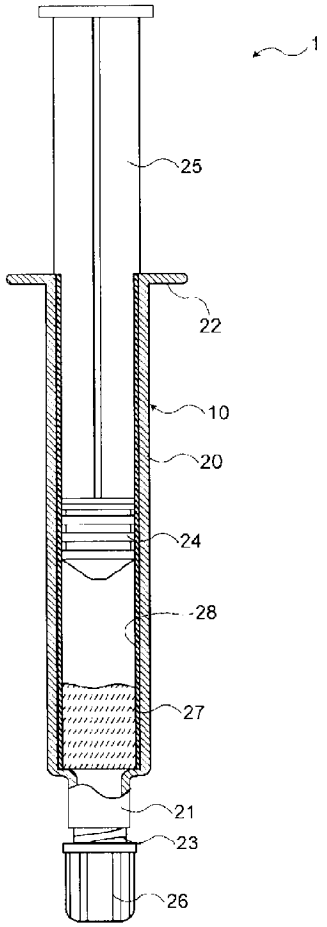


Fig. 1

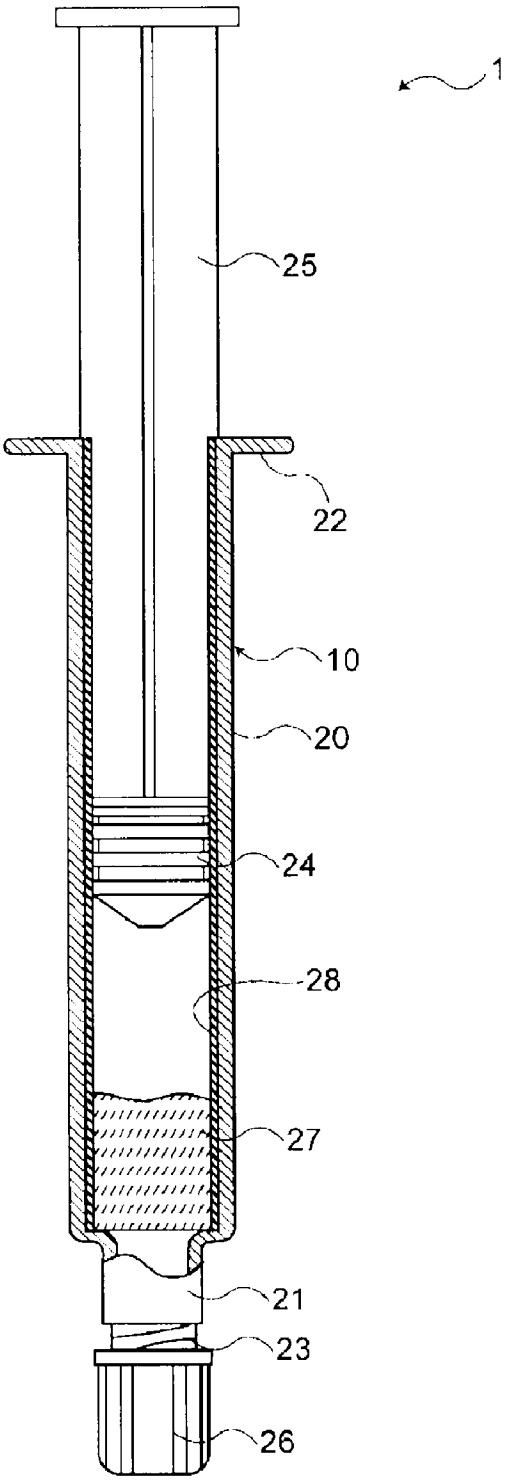
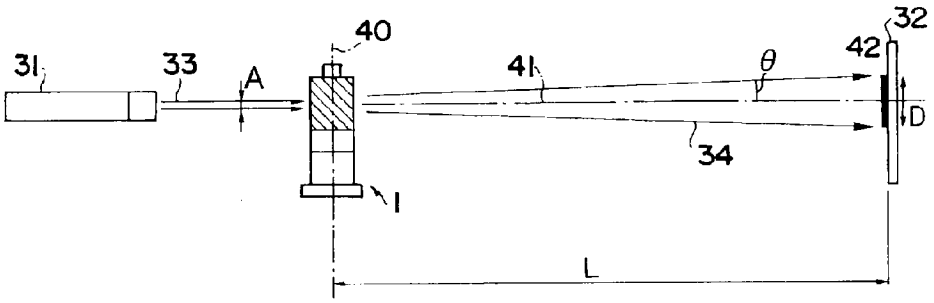


Fig. 2



SYRINGE

TECHNICAL FIELD

[0001] The present invention relates to a syringe, and more particularly relates to a syringe which is excellent in terms of accuracy of visual inspection of the content and a prefilled syringe filled with a high viscosity drug that are suitable for injection of high viscosity drugs.

BACKGROUND ART

[0002] In recent years, prefilled syringes prefilled with drugs have been used for reasons such as prevention of mistakes during medical treatment and prevention of bacterial contamination. A prefilled syringe has the tip opening of a barrel sealed with a cap member, is filled with a drug inside the barrel, has the rear end portion of the barrel sealed with a gasket, and is transported and stored in that state. When administering, an injection needle or an apparatus for administration is attached to the tip of the barrel, and by pushing a plunger attached to the gasket towards the tip and sliding the gasket inside the barrel, the drug flows out from the injection needle and is administered. As such, prefilled syringes have various advantages, such as allowing drugs to be administered in accurate doses without mistakes even during emergencies as there is no need to prepare the drugs at the point of treatment, being highly sanitary as there is no transferring of drugs, and being easy to operate.

[0003] Since prefilled syringes are stored and circulated in a state of being filled with a drug, it may be several years from the filling of the drug in production factories to administration. As such, while it goes without saying that long-term stability is needed, it is also necessary to be able to confirm the safety of the drug by visually inspecting for contamination by impurities. For that reason, the material constituting the barrel needs to be highly transparent, and barrels made of glass, which ensures transparency, have been frequently used in conventional prefilled syringes.

[0004] However, glass barrels crack relatively easily, need to be separated from the other parts and cannot be incinerated together therewith when discarded, and cost more, so there has been a demand for barrels made of resin. Resins with transparency comparable to that of glass barrels have appeared in recent years, and there has been a gradual transition towards resin barrels.

[0005] Regardless of the material of the barrel, to ensure sufficient slidability between the barrel and gasket, a lubricant layer composed of silicone or the like is generally provided on the inner peripheral surface of the barrel and/or the outer peripheral surface of the gasket.

[0006] In the case of conventionally used glass barrels, typically, silicone, in the form of an emulsion, is applied to the inner peripheral surface of the barrels and is fixed by baking at a high temperature (200 to 300° C.). Silicone in itself is not harmful to the human body, but the silicone is fixed to the inner peripheral surface of the barrels to avoid the silicone contaminating the drugs.

[0007] In the case of resin barrels, since the glass transition point of resins is lower than the baking temperature of silicone, the same fixing treatment as for glass barrels cannot be used. In the case of resin barrels, methods in which a radiation or ultraviolet-curable organopolysiloxane is used and methods in which a photopolymerization catalyst such as benzophenone is added to silicone have been proposed as examples of methods for fixing silicone instead of baking at a high temperature (Patent Document 1).

[0008] On the other hand, as methods not involving such a fixing treatment, methods in which a silicone oil is simply applied to the inner peripheral surface of a barrel have also been widely used. In particular, in order to prevent the silicone oil from dripping from the inner peripheral surface of the barrel and contaminating the drug and to suppress increases in the sliding resistance of the gasket, the addition of a fine silica powder to a silicone oil has been proposed (Patent Document 2).

[0009] Additionally, in order to ensure sufficient slidability between the barrel and gasket, a prefilled syringe involving the use of a sealing stopper (gasket) for a syringe, which is a rubber stopper with its surface laminated with a tetrafluoroethylene resin film or an ultrahigh molecular weight polyethylene film, has also been proposed (Patent Document 3).

[0010] Patent Document 1: JP-A 2007-244606

[0011] Patent Document 2: JP-A 2006-94895

[0012] Patent Document 3: JP-A H10-314305

SUMMARY OF THE INVENTION

[0013] However, since methods for the lubrication treatment of resin barrels comprising fixation require a step of curing by radiation etc. as described in the above Patent Document 1, production efficiency is inevitably poor. Additionally, some curing agents etc. may affect the human body when contaminating a drug.

[0014] On the other hand, when the fixing treatment is not performed, naturally, there is a risk of the applied silicone oil separating from the inner peripheral surface of the barrel during filling of a drug, storage or transport and contaminating the drug, causing turbidity. This is, as described in the above Patent Document 2, not a problem that can be completely overcome even when, for example, the silicone oil contains a fine silica powder. Rather, in that case, there is a risk of not only the silicone oil, but also the fine silica powder contaminating the drug.

[0015] Such contamination by the silicone oil from the inner peripheral surface of the barrel is particularly notable when the viscosity of the drug is high. While the exact mechanism is unclear, this is thought to be due to the high shear stress exerted on the silicone oil adhering to the inner peripheral surface of the barrel when filling the syringe with a drug of high viscosity. As mentioned above, silicone oil is not necessarily harmful to the human body, but it is not possible to clearly distinguish between turbidity caused by contamination due to silicone oil and turbidity caused by substantial contamination due to impurities by visual inspection alone, so such syringes may be determined to be defective products during inspection or medical practice and be forced to be discarded without ever being used.

[0016] Further, even when the silicone oil adheres normally to the inner peripheral surface of the barrel, the refractive index of the applied silicone oil differs from the refractive index of the drug and the refractive index of the synthetic resin constituting the syringe, resulting in glare on the inner peripheral surface of the barrel, which may interfere with visual inspection or make it seem as if there has been contamination by impurities or a defect such as a scratch on the barrel.

[0017] Moreover, in the case of the sealing stopper (gasket) for a syringe described in Patent Document 3, since the surface of the rubber stopper is laminated with a resin film, the

error in the inner diameter of the sealing stopper (gasket) for a syringe or the barrel could be increased due to the disparity of the actual dimensions with respect to the dimensions of the original design, and there tended to be problems in the slidability or sealing properties of the sealing stopper (gasket) for a syringe with respect to the inner surface of the barrel.

[0018] As such, there has been a need for syringes capable of reducing the risk of separation and contamination by silicone oil while not requiring fixation of the silicone oil, in which glare rarely occurs on the inner peripheral surface of the barrel, and equipped with sufficient gasket slidability and sealing properties.

[0019] The present invention was achieved in view of the above circumstances, with an object of providing a syringe excellent in inspection accuracy while ensuring slidability and sealing properties between the barrel and gasket, and in particular, a syringe that is also suitable for filling with a high viscosity drug.

[0020] As a result of diligent studies, the present inventors found that by spraying a silicone oil of a predetermined kinematic viscosity onto the inner peripheral surface of a resin barrel at a predetermined application amount per unit area, it is possible to suppress separation and contamination by the silicone oil and glare on the inner peripheral surface of the barrel in addition to providing sufficient slidability.

[0021] That is, the syringe of the present invention is characterized by having a resin barrel, a gasket slidably inserted in the barrel, a plunger attached to the gasket, and a silicone film formed by applying a silicone oil having a kinematic viscosity of 500 to 100,000 cSt to the inner peripheral surface of the above-described barrel in an amount of 5 to 50 μg per 1 cm^2 of area.

[0022] Since a silicone oil having a kinematic viscosity of at least 500 cSt is used as the silicone constituting the silicone film in this syringe, when spraying the silicone oil, the silicone oil is appropriately maintained on the inner peripheral surface of the barrel without running. For that reason, even when a small amount of silicone oil is applied, it is possible to ensure sufficient slidability with the gasket. Additionally, since a silicone oil having a kinematic viscosity of at most 100,000 cSt is used, it can be applied to the inner peripheral surface of the barrel by spraying, and the silicone oil can be evenly applied in the above predetermined application amount per unit area.

[0023] Further, by using a silicone oil having a kinematic viscosity within that range, it is possible to ensure sufficient slidability between the barrel and gasket even when the amount of the silicone oil applied is at most 50 μg per 1 cm^2 of area on the inner peripheral surface of the barrel, and the amount of the silicone oil applied can be suppressed to a low amount. As a result thereof, when filling with a drug, even if the silicone oil becomes mixed into the drug, the amount of contamination can be kept extremely low. As such, the occurrence of turbidity due to contamination by the silicone oil can be suppressed, the causes of turbidity in a drug in a prefilled syringe can be limited to cases of contamination by impurities other than silicone oil, and accuracy in visual inspection to ensure safety can be substantially improved. This is particularly applicable to cases where a high viscosity drug which is susceptible to contamination by silicone oil is loaded. Further, when the application amount is within this range, as long as observation is performed by the naked eye, there is also a low likelihood of glare being detected on the inner peripheral surface of the barrel. Moreover, when the amount of the silicone oil applied to the inner peripheral surface of the barrel is at least 5 μg per 1 cm^2 area, sufficient slidability between the barrel and the gasket can be ensured.

[0024] Since the viscosity of a silicone oil having a kinematic viscosity within the above range is high, it is generally not easy to evenly spray the oil. However, even spraying is possible by appropriately adjusting the liquid temperature, air pressure, nozzle diameter and application time etc. In particular, a fine mist can be sprayed to achieve an extremely thin film such as one within the above range by heating the silicone oil within such a range as not to cause denaturation at the time of spraying.

[0025] Moreover, by designing the maximum outer diameter of the gasket to be greater than the inner diameter of the barrel such that the difference between the maximum outer diameter of the gasket and the inner diameter of the barrel is at least 0.02 mm and at most 0.50 mm, it is possible to suppress drug leakage from the gap between the gasket and barrel while maintaining the sealing properties of the gasket and ensure sufficient slidability between the barrel and gasket.

[0026] Further, as a result of diligent studies, it was found that when, upon shining incident light with an optical axis orthogonally intersecting the central axis of the barrel and measuring the angle of refraction from the optical axis of the transmitted light scattered along the same direction as the central axis, glare on the inner peripheral surface of the barrel can be remarkably suppressed if the angle of refraction is within a predetermined range.

[0027] That is, it was found that the glare could be remarkably suppressed when, upon shining an incident beam with a wavelength of 635 nm to 690 nm and a beam width of at most 3.0 mm on a barrel filled with a drug at an optical axis orthogonally intersecting the central axis of the barrel, the angle of refraction from the optical axis of the transmitted light scattered in the same direction as the above-described central axis was within a range of 0.1 to 0.5°.

[0028] The "angle of refraction" in the present invention refers to the aperture angle from the optical axis of transmitted light scattered along the same direction as the central axis of the barrel of a prefilled syringe filled with a drug when shining an incident beam with an optical axis orthogonally intersecting the central axis of the barrel.

[0029] The barrel of a prefilled syringe will cause a transmitted beam in a direction perpendicular to the central axis to be highly refracted with the center of curvature as the central axis. Accordingly, refraction occurring in the direction perpendicular to the central axis is affected by solely the shape of the barrel, and cannot indicate small variations in the application state of the silicone oil on the inner peripheral surface of the barrel. On the other hand, as the barrel is not substantially curved in the direction of the central axis, the divergence from the optical axis occurring in the same direction as the central axis, i.e. the "angle of refraction" in the present invention, is not significantly affected by the shape of the barrel, and can directly reflect the state of application of the silicone oil.

[0030] It was found that when the angle of refraction of a prefilled syringed filled with a drug is within the range of 0.1 to 0.5°, as long as the observation is performed by the naked eye, there is an extremely low likelihood of glare being detected on the inner peripheral surface of the barrel. As such,

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