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Stabilized Liquid Antibody Formulations for Parenteral Administration

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Patent pending; available for licensing.

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Background

Instabilities of proteins are a major obstruction to commercial development of protein drugs. In particular, protein aggregation, which often arises because of this instability, is a major obstacle in all phases of drug development. This is particularly important for multi-domain proteins such as monoclonal antibodies (mAbs), which are popular drug candidates due to high binding affinities and specificities and the ease with which they can be targeted to specific antigens.

Liquid formulations for antibodies are the goal for most therapeutic products. However, achieving sufficient shelf life of a liquid formulations is often precluded by the aggregation of the protein. This problem is particularly difficult because of the relative high doses for mAbs and the need to have concentrations of 100 mg/ml or higher. In addition to aggregation, high concentration formulations are prone to liquid-liquid phase separation, opalescent appearance and/or high viscosity. The current invention provides a means by which to minimize aggregation, while avoiding phase separation or opalescent and providing an appropriate viscosity.

Technology

A University of Colorado research group led by Theodore Randolph and John Carpenter has developed a technique for concentration and production of stable, ready-to-use liquid formulations of any antibody that exhibits certain phase behaviors, as well as methods to identify which antibodies can be formulated using these techniques. These antibody formulations may be therapeutic or prophylactic antibodies, useful in the treatment and/or management of various diseases; these formulations can also be used to diagnose, detect or monitor disease associated with various disease conditions. Proof of concept studies were demonstrated using proprietary mAbs, though this technique is not limited to the antibodies tested. The stable liquid formulations of antibodies exhibit stability, low to undetectable levels of antibody fragmentation and/or aggregation, and very little to no loss of the biological activities of the antibodies (including antibody fragments thereof) during manufacture, preparation, transportation, and storage, as assessed by, for example, high performance size exclusion chromatography (HPSEC).

Advantages

- ⇒ Technology applicable to any antibody exhibiting certain phase behaviors
- ⇒ Antibody preps demonstrate low to undetectable levels of antibody fragmentation and aggregation
- ⇒ Very little or no loss of antibody's biological activity during manufacturing
- ⇒ Increased stability and shelf life of concentrated antibody-based therapeutics
- ⇒ Reduced waste associated with unused portions
- ⇒ Quicker and easier administration by medical personnel
- ⇒ Faster, less costly manufacturing process

Key publication: "Understanding and modulating opalescence and viscosity in a monoclonal antibody formulation." J Pharm Sci. 2009 May 27.

Patent application: "Stabilized Antibody Formulations and Uses Thereof." 9/25/2007.