Formulation, Characterization, and Stability of Protein Drugs, Rodney Pearlman and Y. John Wang, eds., Plenum Press, New York (1996), U.S. Patent No. 5,919,757 to Michaelis *et al.*, and U.S. Patent No. 6,908,610 to Sato *et al.* Traditionally, surfactants are included in hG-CSF formulations and may protect hG-CSF at potentially destabilizing interfaces, against surfaces encountered during processing, and against the alteration of its conformational stability.

The cDNA cloning and expression of recombinant bovine G-CSF (bG-CSF) has also been described. For example, the polynucleotide and polypeptide sequence of mature bG-CSF is presented in U.S. Patent No. 5,849,883, which also describes methods to clone, isolate, and purify the polypeptide and analogs thereof. Mature bG-CSF is 174 amino acids in length and has 82% homology to hG-CSF. Heidari *et al.*, *supra*, describe the expression, purification, and biological activities of bG-CSF.

Administration of bG-CSF to cattle can provide therapeutic benefits. Accordingly, a pharmaceutical formulation containing bG-CSF is desirable to utilize its therapeutic potential. However, bG-CSF pharmaceutical formulations developed according to traditional methods known in the art result in undesirable product properties, such as aggregation and destabilization of the bG-CSF polypeptide and/or the formulation.

Therefore, there exists a need for a stable bG-CSF pharmaceutical formulation with desirable properties, such as minimal product aggregation and destabilization properties. Accordingly, the present invention provides stable aqueous pharmaceutical formulations with a bG-CSF polypeptide or a variant thereof which exhibit desirable properties and provide related advantages as well.

SUMMARY

In an aspect, there is provided a stable aqueous formulation comprising bG-CSF-T133pAF-20K PEG, a citrate or succinate buffer, arginine, and optionally a counter ion for arginine, and wherein said formulation contains less than 0.001% of a surfactant.

In another aspect, there is provided the use of the formulation as defined above in the manufacture of a medicament for treating an animal having a disorder modulated by bG-CSF.

DETAILED DESCRIPTION

This invention provides stable aqueous formulations comprising a bG-CSF polypeptide or a variant thereof, a buffer substance, and an excipient, wherein said formulation is substantially free of polyoxyethylene (20) sorbitan monolaurate. The invention also provides methods of using, a lyophilized or powdered form of, and processes for preparing the formulation.