Q-dextran

CAS nr: N/A

Chemical name: 2-hydroxypropyl-trimethylammonium-dextran chloride

Structure:

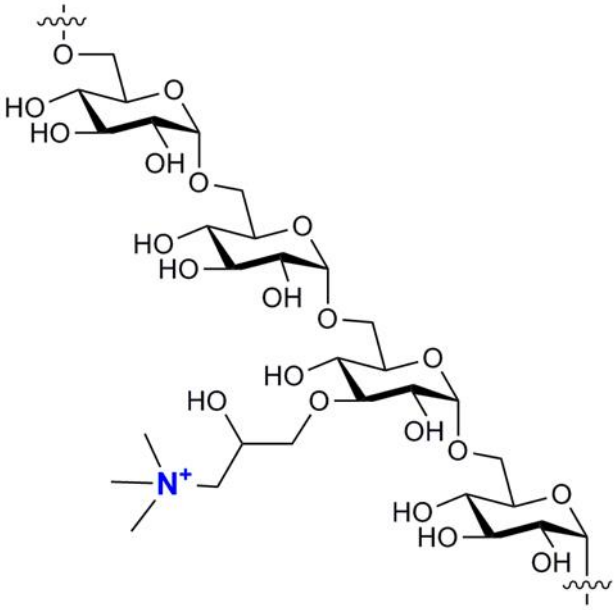

Fig. 1. Structure of fragment of Q-dextran. Q-dextrans contain only quaternary amine groups. These derivatives are very soluble in water and electrolyte solutions and are supplied as white powders.

Synthesis and structure

Q-dextrans are synthesised by reacting dextran fractions with 2,3-epoxypropyltrimethylammonium chloride (1–3). After purification, the products are controlled for Mean molecular weight (Mw, Mn), solubility, degree of substitution, and loss on drying. A specification may be obtained on request.

The products are designated by the approximate molecular weights of the dextran fractions used. Thus, for example, the product Q-dextran 70 has a molecular weight (Mw) of approx. 70 000. The actual molecular weight is determined by gel permeation chromatography (GPC). This value is supplied with the Certificate of Analysis. The differences between the Mw values of the starting dextran fraction and the final product depend on changes in the hydrodynamic volume of the molecules after substitution. The dextran used is from Leuconostoc mesenteroides B-512F which is essentially a linear α-(1-6)-linked glucose chain with however a low percentage (2-5%) of α-(1-3) branches distributed along the chain4. The dextran fractions used are from weight average molecular weights (Mw) of 4000 to 2000000 and are carefully controlled by GPC, absorbance, nitrogen content, pH, specific optical rotation and loss on drying.

Physical and chemical properties

These derivatives are very soluble in water and electrolyte solutions and are supplied as white powders. Q-dextrans contain only quaternary amine groups (see Fig.1). Unlike DEAE-dextrans, Q-dextrans will be positively charged over the normal range of use for dextrans (pH 4-10). The nitrogen content is approx. 2% (by elemental analysis) which corresponds to approximately one quaternary ammonium group for every four glucose units. It can be inferred from the molecular weight determinations (GPC), that the hydrodynamic volumes of Q-dextrans do not differ greatly from dextran itself. These products will have a much stronger net charge than corresponding DEAE-dextrans and thus give enhanced responses in systems where this effect is important (5,6). The product has a pronounced cationic character by virtue of quaternary ammonium substituents and will exhibit affinity to polyanionic surfaces or molecules (5,6). Q-dextrans are insoluble in most organic solvents, for example, ethanol, methanol, acetone, chloroform, ethyl acetate, and diethyl ether. The solution properties of cationic polymers have been widely studied, mostly by viscometry – a few examples are listed below (5,6).

Stability

No formal stability studies on Q-dextrans have been reported. However, the stability of DEAE-dextran is well-documented and since this closely resembles Q-dextran, we can presume that its quality and efficacy will be maintained for more than three years when stored at room temperature. It is recommended that the products are stored in air-tight containers in the dark.

Applications

Polycationic polysaccharides have been found to induce many interesting effects in biological systems presumably due to their cationic character and interactions with tissue and cell surfaces, which generally possess an overall negative charge. A random selection of references on various fields of application for polycationic dextrans is presented below.

Enhanced uptake by cells (transfection)

Many reports testify to the enhanced uptake of viral nucleic acids by cells in the presence of DEAE-dextran without detrimental effects on the cells (7–9). Only at higher concentrations may such effects be apparent.

Adjuvant in vaccines

There are numerous reports on the efficacy of cationic-dextran in veterinary vaccine production in lambs, calves and piglets (10–12).

Agent for gene therapy

Numerous reports described potential applications of cationic-dextran for gene therapy (13).

Stabilizer for protein storage

DEAE-dextran has been shown to stabilize lyophilized proteins (e.g. enzymes) and also protein solutions. Further improvements may be achieved by using a combination of DEAE-dextran and a polyalcohol (14–17).

Agent for drug delivery

The electrostatic binding properties of cationic-dextran to polyanions is well established and has been used to present drugs and similar agents in a form that mediates the uptake of the agent in vivo (18-20). Recent studies penetrate the factors influencing complex formation and properties of the complexes (21,22).

Flocculating agent

Many cationic polysaccharides showed high flocculating efficiency when used at optimal flocculant doses. The charge density of the polycations determines the efficacy for reaching the maximum degree of clarity (23).

Bile acid sequestrant

The binding of various bile acids to dextran gels with pendant quaternary ammonium substituents was studied. The binding constants were found to be more than 20 times higher than for other commercial resins (24).

References

1. M. Antonietti, Intrinsic viscosity of small spherical polyelectrolytes: Proof for the intermolecular origin of the polyelectrolyte effect; J Chem. Phys. 1996, V105, P7795 CAPLUS
2. M.Antonietti, Solution Viscosity of Polyelectrolyte-Surfactant Complexes: Polyelectrolyte Behavior in Nonaqueous Solvents, Macromolecules 1995, V28, P2270 CAPLUS
3. M. Antonietti, Quantitative description of the intrinsic viscosity of branched polyelectrolytes, Macromolecules, 1997, V30, P2700 CAPLUS
4. L.G.Ahrgren and A.N.de Belder, Dextran or cross-linked dextran having quaternary amino-groups, E.P. 66135, 1982; U.S. 4,591,638 , 1986.
5. T.Heinze, v.Haack and S.Rensing, Starch derivatives of high degree functionalization. 7. Preparation of cationic 2-hydroxypropyltrimethylammonium chloride starches, Starch/Stärke, 2004, 56, 288-296
6. A.Ebringerová, Z.Hromádková, M.Kacuráková etal., Quaternized xylans; synthesis and structural characterization, Carbohydr. Polym., 1994, 24, 301-308.
7. L.Ghimici, M. Nichifor, and B. Wolf, Ionic Polymers Based on Dextran: Hydrodynamic Properties in Aqueous Solution and Solvent Mixtures J. Phys. Chem. B, 2009, 113(23), 8020-80.
8. R.F.Selden, Transfection using DEAE-dextran, Curr.Protoc.Immunol., 2001, chap.10: Unit 10.14.
9. T.Gulick, Transfection using DEAE-dextran, Curr.Protoc.Immunol., 2001, chap.9: Unit 9.2.
10. J.S.Pagano and A.Vaheri, Enhancement of infectivity polio virus RNA with DEAEdextran, Arch.Gesamte Virusforsch., 1965, 14, 456-464,
11. M.Fiala and B.Salzman, Enhancement of rhinovirus ribonucleic acid by DEAEdextran, Appl. Microbiol., 1969, 17, 190-191.
12. S.I.Westbrook and G.H.McDowell, Immunization of lambs against somatotropin release inhibiting factor to improve productivity; Comparison of adjuvants, Aust.J.Agric.Res., 1994, 45, 1693-1700.
13. K.J.Beh and A.K.Lascelles, The effect of adjuvants and prior immunization on the rate and mode of uptake of antigen into afferent popliteal lymph from sheep, Immunol., 1985, 54, 487-495.
14. M.Hibma and J.F.T.Griffin, The effect of adjuvants on active and passive immunityn pregnant deer and their offspring, Vet.Immunol.Immunopath., 1992, 31, 279-287.
15. J.M.Kaplan, et al., Hum.Gene Ther., 1998, 9, 1469-79.
16. S.Liptay, H.Weidenbach, et al., Digestion, 1998, 59, 142-14.
17. L.Feng, L.Zhang et al., Roles of dextrans on improving lymphatic drainage for liposomal drug delivery, J.Drug Target., 2010, 18(3), 168-78.
18. F.Uchiumi, T.Watanabe and S.Tanuma, Characterisation of various promoter regions of the human DNA helicase-encoding genes and identification of duplicated ets(GGAA) motifs as an essential transcription regulatory element, Exp.Cell Res., 2010, 316(9), 1523-34.
19. T.D.Gibson, Protein stabilisation using additives based on multiple electrostatic interactions, Dev.Biol.Stand., 1996, 87,207-17.
20. V.G.Gavalas, N.A.Chaniotakis and T.D.Gibson, Improved operational stability of biosensors based on enzyme-polyelectrolyte complex adsorbed into a porous carbon electrods, Biosens. Bioelectron., 1998, 13(11), 1205-11.
21. N.A.Chaniotakis, Enzyme stabilization strategies based on electrolytes and polyelectrolytes for biosensor applications, Anal.Bioanal.Chem., 2005, 378(1), 89-95.
22. US Patent 6,133,229 (2000)

23. Delivery Technologies for Biopharmaceuticals; Peptides, Proteins, Nucleic acids and Vaccines; Lene Jörgensen(ed), Wiley, 2009, p.343.
24. L.Feng, LZhang, M.Lui et al., Roles of dextrans in improving lymphatic drainage for liposomal drug delivery, J.Drug Target., 2010, 18(3), 168-78.
25. A.O.Abioye and A.Kola-Mustapha, Controlled electrostatic self-assembly of ibuprofen-cationic dextran nanoconjugates prepared by low energy green process – a novel drug delivery tool for poorly soluble drugs, Pharm.Res., 2014, Dec 20 (Epub).
26. D.Le Cerf, A.S.Pepin and P.M.Niang, Formation of polyelectrolyte complexes with DEAE-dextran; Charge ratio and mol. mass effect, Carbohydr. Polym., 2014, 113, 217-224.
27. Y.Kikuchi and K.Hori, Structure and properties of polyelectrolyte complex prepared from DEAE-dextran and poly(sodium glutamate), Nippon Kagsku Kaishi, 1982, 5, 847-52.
28. L.Ghimici and M.Nichifor, Flocculation Properties of Some Cationic Polysaccharides, J. Macromol. Sc., Part B: Physics, 2009, 48(1), 106-113.
29. M. Nichifor, X.X.Zhu, W.Baille, et al., Bile acid sequestrants based on cationic dextran hydrogel microspheres. 2. Influence of the length of alkyl substituents at the amino groups of the sorbents on the sorption of bile salts, J. Pharm. Sc., 2001, 90(6), 681-689