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Study of conformational properties of cereal β-glucans by computer modeling

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ABSTRACT

Molecular modelling was used to study the conformational properties of cereal β-glucans and compared with experimental results. Followed the steps of exploring global minima of β 1-4 and β 1-3 linked disaccharides and building up the repeating units, the consecutive cellotriosyl units, which are considered as reaction sites of β-glucan chains, were created and then characterized as a three fold helix with a pitch of 41.35 Å. Mostly importantly, the 3D molecular model of cereal β-glucans was created and the moderately extended sinuous chain conformation was first visualized. The conformational parameters of cereal β-glucans were calculated by RMMC simulation, which are in good agreement with experimental results. The calculated parameters also revealed that the chain stiffness of β-glucans increased with the tri/tetra ratio.

1. Introduction

Cereal β-glucan is a cell wall polysaccharide in the grains of cereals, including oats, barley, rye and wheat. The structural feature of cereal β-glucans is typical of a linear mixed β 1-4, β 1-3 linked homoglucan. Cereal β-glucans have been accepted as functional, bioactive ingredients. However, the mechanisms of how they provide beneficial physiological effects and exhibit functional properties are still not clear. In a recent review (Wood, 2003), the relationships between the solution properties of cereal β-glucans and observed physiological effects have been discussed. It was concluded that the efficacy of various soluble fibre preparations could not simply be related to the amount of β-glucan, as there are presently insufficient data to allow evaluation. Even though some progresses have been achieved for establishing the structure–function relationship (Lazaridou, Biliaderis, Micha-Screttas, & Steele, 2004; Li, Cui, & Kakuda, 2006; Tosh, Brummer, Wood, Wang, & Weisz, 2004), the detailed information and mechanisms are still not clear. To explore these mechanisms, it is essential to get an insight understanding of the conformational properties of cereal β-glucans.

Light scattering is the most used method for conformational study of polysaccharides. However, a new method of computer modelling has been accepted as an important tool for conformational studies of polysaccharides recently. Compared with other methods, such as light scattering, an explicit conformation of polysaccharide can be obtained and visualized. Furthermore, the arbitrarily designed virtual molecules are more favourable to study the structure–conformation relationship. In contrast, it is almost impossible to obtain these ideal molecules from experimental methods.

Some of the methods for calculating the conformational properties of polymer chains are based upon the rotational isomeric state (RIS) theory (Flory, 1969). However, there are difficulties with the application of RIS in a reliable manner to polymers with complex monomeric structures, especially for polymers containing rings along the chain backbone. A new method, RIS Metropolis Monte Carlo (RMMC), was recently developed by Honeycutt (1998). The RMMC method, employed with a reasonably well-parameterized force field, is especially useful for implementation on complicated polymer structures containing rings in the backbone for which formulation of the RIS model can some times not be straightforward to perform. Like traditional RIS method, only torsional degrees of freedom are considered in determining a chain's conformation; bond length and angles are fixed. Unlike RIS and RIS Monte Carlo calculations, RMMC does not use statistical weights. Instead, it uses the energy as computed from a force field in order to calculate chain conformational properties. The only energy terms considered in an RMMC calculation are torsion, van der Waals, and Coulombic (electrostatic) terms. Furthermore, RMMC allows torsion angles to vary continuously; it does not impose the assumption of discrete rotational states. RMMC simulations provide an effective method to the calculation of the overall

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chain dimensions such as the mean-squared end-to-end distance ($\langle r^2 \rangle$), the radius of gyration (R_g), the persistence length (L_p) and the characteristic ratio (C_∞).

In present study, RMMC method was used to investigate the conformational properties of cereal β-glucans and characterize the reaction sites along the polymer chain, which is responsible for physiological effects and functionalities of cereal β-glucans. Before RMMC simulation, molecular mechanics and dynamics were used for energy minimization to obtain the relaxed conformations of cereal β-glucan molecules. The conformational parameters such as persistence length, radius of gyration, and characteristic ratio, etc. were then calculated after RMMC simulation. These parameters were compared with experimental results.

2. Computational methods

The glycosidic dihedral angles are defined according to the IUPAC–IUB (1997) heavy-atom convention: For (1→4) glycosidic linkages, Φ = O-5′–C-1′–O-4–C-4 and Ψ = C-1′–O-4–C-4–C-5. or Φ_H is defined Φ_H = H-1′–C-1′–O-4–C-4 and Ψ_H = C-1′–O-4–C-4–H-4 (Fig. 1). The primed atoms correspond to the non-reducing residue and the unprimed atoms correspond to the reducing one. The orientation of the primary hydroxyl groups (ω) is referred to as either *gauche–trans* (*gt*), *gauche–gauche* (*gg*) or *trans–gauche* (*tg*). Using this terminology, one first states the torsion angle defined as ω (O(5)–C(5)–C(6)–O(6)), followed by C(4)–C(5)–C(6)–O(6). For the graphical representation of all oligomers, the starting geometries of the monomeric units were derived from the library of the software package Insight II (Molecular Simulation, Inc.).

Geometry optimization was performed using the molecular modelling package Insight II of MSI (Version 4.0.0) and a Silicon Graphic O2 workstation. The Amber-H force field of Homans (1990) contains a correction for the anomeric and exo-anomeric effects and has been specially adapted for the study of carbohydrates. For exploring energy-relaxed conformational Φ–Ψ maps, the glycosidic dihedral angles were restrained by a cosine type potential with a force constant of 100 kcal mol^{-1}. The energy minimizations were performed by the initial 300 steps of Steepest descent method followed by the Polak–Ribiere conjugate gradient method, and then the final Quasi-Newton (BFGS) method with the default energy convergence criterion of 0.001 kcal/mol. In order to mimic the solvation effects, a dielectric constant, $\epsilon = 80$, was used in the calculations.

The conformational spaces of cellobiose and laminarabiose were explored by systematically stepping the glycosidic Φ and Ψ torsion angles from −180° to 180° with 20° increments. At each point, energies were calculated after energy minimization with restraints for those Φ and Ψ torsion angles, but while allowing the other variables to relax. Because of the well-known multiple-minima problem of the potential-energy hypersurface due to the large number of degrees of freedom, together with the inherent limitations of the minimization procedures, emphasis is placed on the importance of drawing adiabatic maps by using starting geometries with different orientations of the pendant groups. Adiabatic maps were plotted by taking into account the lowest energy conformer at each (Φ, Ψ) point. A systematic method was adopted from Dowd et al. (Dowd, French, & Reilly, 1992) as described below. Sixteen starting structures were used at each Φ and Ψ point for each disaccharide. These structures were all composed of $^4C_1$ D-glucopyranose rings, but varied in the conformations of exocyclic side-groups. The hydroxymethyl groups had either *gauche–trans* (*gt*) or *gauche–gauche* (*gg*) orientations, with their hydroxyl hydrogen atoms oriented to weakly hydrogen bond with the ring oxygen atom. *Trans–gauche* hydroxymethyl orientations (*tg*) were not considered, since they are not found in structures determined by single-crystal methods or as significant conformers in solution. The secondary hydroxyl groups were likely to form a crown of cooperative hydrogen bonds, oriented either clockwise (*c*) or reverse clockwise (*r*) around the pyranose ring (Ha, Madsen, & Brady, 1988). These orientations place hydroxyl hydrogens in favourable positions to forming hydrogen bond network. For the reverse-clockwise orientation, for example, the torsion angle C(3)–C(2)–O(2)–H(O2) is 180°.

Inspection of the energy landscapes allowed the identification of global minima of torsion angles. The torsion angle parameters of the global minima were used to build an initial model of trisaccharide and tetrasaccharide repeating units of cereal β-glucans. The initial conformation of repeating units was relaxed by energy minimization. Solvent simulation approach was taken for structure calculation and further refinement. The repeat units were immersed in an equilibrated water box of dimensions 60 × 30 × 30 Å^3 (1571 water molecules), and the system was set up as a periodic boundary condition simulation with group-based summation (15.0 Å cut off, 2.0 Å spine, 1.0 Å buffer) and $\epsilon = 1$. After solvation, 1000 steps minimization were done to the ensembles to relax steric overlaps. A preliminary simulation was performed for 10 ps to allow further relaxation of the solvent molecules. Subsequently, the production MD simulations were done for 300 ps. The system was kept at constant volume and 298 ± 10 K by the Velocity-scale method as implemented in DISCOVER 97.0

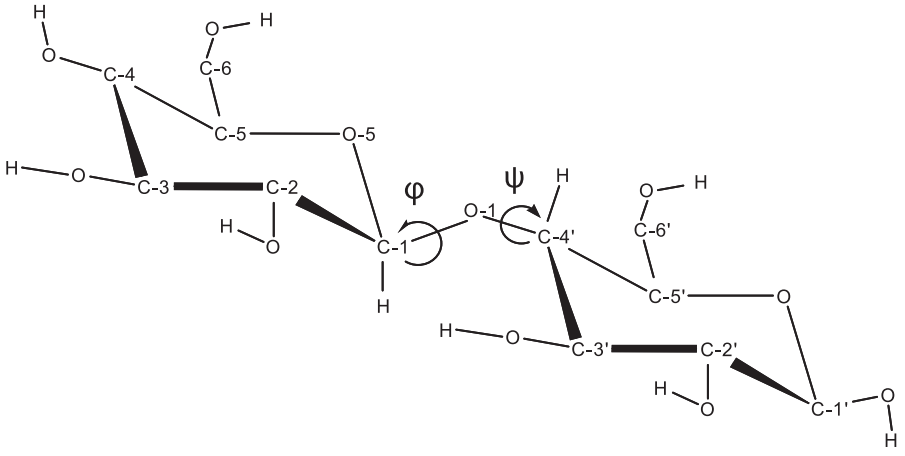

Fig. 1. Definition of the torsion angles Φ and Ψ in β-cellobiose.