A novel heterogalactan from Antrodia camphorata and antiangiogenic activity of its sulfated derivative postprint

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Abstract

Antrodia camphorata, a rare and expensive mushroom native to Taiwan has been considered to own diverse medicinal benefits. To obtain the homogeneous polysaccharide ACW0 and evaluate its biological functions, the lyophilized powders of A. camphorata mycelium were extracted with hot water and purified by anion exchange and gel permeation chromatography. The single symmetrical peak appeared on HPGPC indicated the homogeneous polysaccharidewe have got and its molecular weight was also estimated to be 14.5kDa. Based on monosaccharidecomposition by GC, ACW0 predominantly contained galactose (94.98%),traces of mannose (2.41%), andfucose (2.61%). The polysaccharide was shown to be a mannofucogalactan withabackbone chain of -D-1,6-linked Gal, nonreducing terminal -D-Man and -L-Fuc substituted at O-2 for nearly every six -D-1,6-linked Gal. The bioactivity study indicated that the native polysaccharide ACW0 had no inhibition on in vitro matrigel tube formation, thereby ACW0 was sulfated, designated as ACW0-Sul, to change its chemical structure. The degree of sulfation was calculated to be 2.43, suggesting that almost every sugar residue was fully sulfated and sulfation position was also determined by the obvious change of chemical shiftsin the 13C NMR spectrum. We find that C-2,C-3 and C-4 of 1,6-linked Gal, C-3 and C-4 of 1,2,6-linked Gal were sulfated. However, the peaks of terminal Man and Fuc disappeared, which possibly indicated the degradation of them during sulfation. Most importantly, the sulfate derivative ACW0-Sul could disrupt tube formation and inhibit the migration of human microvascular endothelial cells (HMEC-1) dose-dependently. Besides, phosphorylation of ErK and FAK were also significantly inhibited by ACW0-Sul. These results suggested that introduction of sulfate group could enhance the bioactivity of polysaccharide from A. Camphorataand its sulfate derivative could be a potent antiangiogenic inhibitor for anti-cancer therapy.

Full Text

A Novel Heterogalactan from *Antrodia camphorata* and Antiangiogenic Activity of Its Sulfated Derivative

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Abstract: *Antrodia camphorata*, a rare and expensive mushroom native to Taiwan, has been considered to possess diverse medicinal benefits. To obtain the homogeneous polysaccharide ACW0 and evaluate its biological functions, lyophilized powders of *A. camphorata* mycelium were extracted with hot water and purified by anion exchange and gel permeation chromatography. A single symmetrical peak appeared on HPGPC, indicating the homogeneity of the obtained polysaccharide, and its molecular weight was estimated to be 14.5 kDa. Based on monosaccharide composition analysis by GC, ACW0 predominantly contained galactose (94.98%), with traces of mannose (2.41%) and fucose (2.61%). The polysaccharide was characterized as a mannofucogalactan with a backbone chain of -D-1,6-linked Gal, non-reducing terminal -D-Man and -L-Fuc substituted at O-2 for nearly every six -D-1,6-linked Gal residues.

Bioactivity studies indicated that the native polysaccharide ACW0 exhibited no inhibition of in vitro Matrigel tube formation. Therefore, ACW0 was sulfated, designated as ACW0-Sul, to modify its chemical structure. The degree of sulfation was calculated to be 2.43, suggesting that almost every sugar residue was fully sulfated. The sulfation positions were also determined by significant changes in chemical shifts in the ^{13}C NMR spectrum. We found that C-2, C-3, and C-4 of 1,6-linked Gal, and C-3 and C-4 of 1,2,6-linked Gal were sulfated. However, the peaks corresponding to terminal Man and Fuc disappeared, possibly indicating their degradation during sulfation.

Most importantly, the sulfated derivative ACW0-Sul could disrupt tube formation and inhibit the migration of human microvascular endothelial cells (HMEC-1) in a dose-dependent manner. Furthermore, phosphorylation of ErK and FAK was also significantly inhibited by ACW0-Sul. These results suggest that introduction of sulfate groups could enhance the bioactivity of polysaccharides from *A. camphorata*, and its sulfated derivative could serve as a potent antiangiogenic inhibitor for anticancer therapy.

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Note: Figure translations are in progress. See original paper for figures.