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Momordica charantia polysaccharides could protect against cerebral ischemia/reperfusion injury through inhibiting oxidative stress mediated c-Jun N-terminal kinase 3 signaling pathway

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ABSTRACT

Momordica charantia (MC) is a medicinal plant for stroke treatment in Traditional Chinese Medicine, but its active compounds and molecular targets are unknown yet. *M. charantia* polysaccharide (MCP) is one of the important bioactive components in MC. In the present study, we tested the hypothesis that MCP has neuroprotective effects against cerebral ischemia/reperfusion injury through scavenging superoxide (O_2^-), nitric oxide (NO) and peroxynitrite ($ONOO^-$) and inhibiting c-Jun N-terminal protein kinase (JNK3) signaling cascades. We conducted experiments with *in vivo* global and focal cerebral ischemia/reperfusion rat models and *in vitro* oxygen glucose deprivation (OGD) neural cells. The effects of MCP on apoptotic cell death and infarction volume, the bioactivities of scavenging O_2^-, NO and $ONOO^-$, inhibiting lipid peroxidation and modulating JNK3 signaling pathway were investigated. Major results are summarized as below: (1) MCP dose-dependently attenuated apoptotic cell death in neural cells under OGD condition *in vitro* and reduced infarction volume in ischemic brains *in vivo*; (2) MCP had directing scavenging effects on NO, O_2^- and $ONOO^-$ and inhibited lipid peroxidation; (3) MCP inhibited the activations of JNK3/c-Jun/Fas-L and JNK3/cytochrome C/caspases-3 signaling cascades in ischemic brains *in vivo*. Taken together, we conclude that MCP could be a promising neuroprotective ingredient of *M. charantia* and its mechanisms could be at least in part attributed to its antioxidant activities and inhibiting JNK3 signaling cascades during cerebral ischemia/reperfusion injury.

1. Introduction

Free radicals, including reactive oxygen species (ROS) and reactive nitrogen species (RNS), are important players in cerebral ischemia-reperfusion injury. Brain ischemia and reperfusion insults can produce large amount of ROS and RNS (Clemens, 2000; Sugawara and Chan, 2003). When beyond the capacity of antioxidant systems, excessive free radicals trigger numerous molecular and cellular cascades to mediate inflammation and cell death, subsequently inducing blood–brain-barrier (BBB) hyperpermeability, brain edema and infarction enlargement (Chan, 2001; Pun et al., 2009). High concentration of NO, derived from the activation of nNOS and *de novo* synthesis of iNOS, can induce apoptotic cell death (Dalkara et al., 1998), increase infarction

Abbreviations: MCP, *Momordica charantia* polysaccharides; JNK3, c-Jun N-terminal kinase 3; I/R, ischemia/reperfusion; 4-VO, four-vessel occlusion; MCAO, middle cerebral artery occlusion; $ONOO^-$, peroxynitrite; O_2^-, superoxide; NO, nitric oxide; SD, Sprague–Daweley; SDS-PAGE, sodium dodecyl sulfate-polyacrylamide gel electrophoresis.

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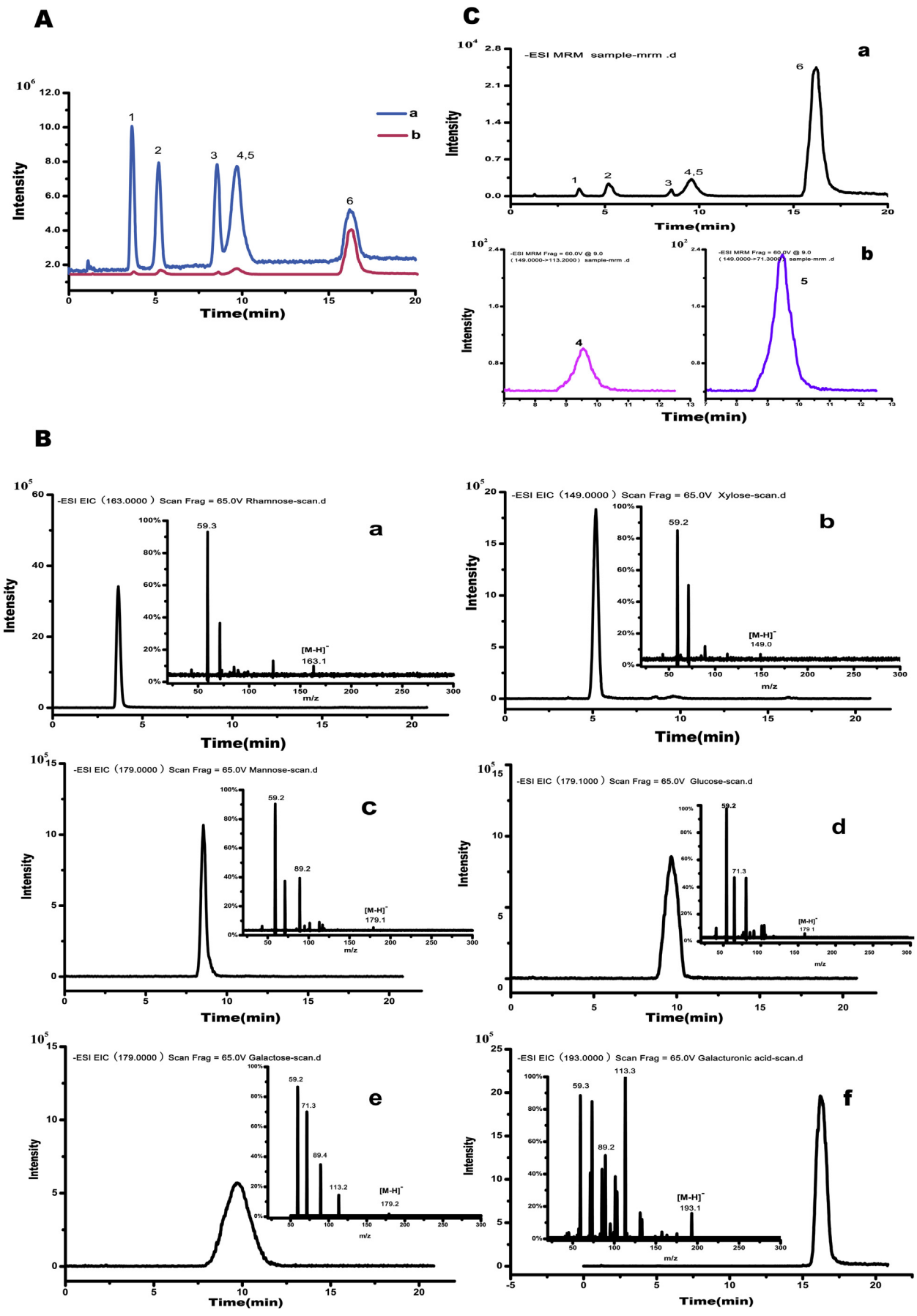

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