

Silymarin- and melatonin-mediated changes in the expression of selected genes in pesticides-induced Parkinsonism

Naveen Kumar Singhal · Amit Kumar Chauhan ·
Swatantra Kumar Jain · Rishi Shanker ·
Chetna Singh · Mahendra Pratap Singh

Received: 3 June 2013 / Accepted: 9 August 2013 / Published online: 22 August 2013
© Springer Science+Business Media New York 2013

Abstract Parkinson's disease (PD) is the second most unconcealed neurodegenerative disorder labelled with motor impairments. Two pesticides, manganese ethylene-1,2-bisdithiocarbamate (maneb) and 1,1'-dimethyl-4,4'-bipyridinium dichloride (paraquat), together, are reported to increase the incidence of PD in humans and Parkinsonism in mice. Conversely, silymarin and melatonin, two naturally occurring antioxidants, rescue from maneb- and paraquat-induced Parkinsonism. The study examined silymarin- and melatonin-mediated changes in the expression of selected genes in maneb- and paraquat-induced Parkinsonism employing mouse discover chips microarrays. The mice were treated intraperitoneally (i.p.), daily, with silymarin (40 mg/kg) or melatonin (30 mg/kg) for 9 weeks along with vehicles. Subsets of animals were also treated with maneb (30 mg/kg; i.p.) and paraquat (10 mg/kg; i.p.), twice a week, for 9 weeks. Whilst the expression of genes in the striatum was determined by microarray, the expression of randomly selected transcripts was validated by quantitative real-time polymerase chain reaction (qRT-PCR). Combined maneb- and paraquat-treatment altered

the expression of several genes associated with apoptosis, inflammation, cell cycle, cell-signalling, etc. pathways. Silymarin and melatonin significantly resisted the changes in the expression of a few genes related to apoptosis, inflammation, cell cycle, cell-signalling, etc. The expression patterns of seven randomly selected genes were analyzed by qRT-PCR, which were found to follow the similar trends, as observed with microarray. The results obtained from the study thus demonstrate that despite resemblances, silymarin and melatonin differentially offset maneb- and paraquat-induced changes in transcriptome.

Keywords Parkinson's disease · Maneb · Paraquat · Silymarin · Melatonin · Microarray

Introduction

Parkinson's disease (PD) is a complex neurological disorder, characterized by the striatal dopamine deficiency, nigrostriatal dopaminergic neurodegeneration and motor impairments [1, 2]. PD is mainly linked with the advanced age but the roles of environmental exposure to pesticides and genetic makeup of an individual have been lately appreciated [1–3]. Maneb, a fungicide, and paraquat, an herbicide, have been implicated in PD pathogenesis through epidemiological and animal studies [1–7]. Maneb crosses the blood–brain barrier owing to its lipophilic nature while paraquat crosses it through the neutral amino acid transporter [2, 3, 7]. Maneb is reported to inhibit the mitochondrial complex III in a few reports but most of the studies did not observe any change in complex III activity. On the other hand, paraquat is consistently reported to inhibit the mitochondrial complex I [2, 3, 5, 7]. These two pesticides together induce more pronounced oxidative

Naveen Kumar Singhal and Amit Kumar Chauhan contributed equally to this work.

N. K. Singhal · A. K. Chauhan · R. Shanker · C. Singh ·
M. P. Singh (✉)
CSIR-Indian Institute of Toxicology Research, Mahatma Gandhi
Marg, Post Box 80, Lucknow 226 001, Uttar Pradesh, India
e-mail: singhmahendrapratap@rediffmail.com

A. K. Chauhan · C. Singh
Academy of Scientific and Innovative Research, New Delhi,
India

S. K. Jain
Jamia Hamdard, New Delhi 110 062, India