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Neuroprotective role of curcumin and resveratrol combination against AlCl3 induced Alzheimer's disease in rats

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Clinical and experimental studies have demonstrated that chronic exposure of Aluminum, proposed as an environmental factor, may affect several enzymes and other biomolecules related to neurotoxicity and Alzheimer's disease (AD). APE1 a multifunctional protein, functions in DNA repair and plays a key role in cell survival versus cell death upon stimulation with cytotoxic agent, making it an attractive emerging therapeutic target. The objective of the present study was to assess potential of curcumin and resveratrol to treat oxidative stress in neuronal death and inflammation in Alzheimer's disease of $AlCl_3$ induced rat models. Wistar rats were treated with aluminum chloride (25 mg/kg $AlCl_3$ daily by oral gavage) for 28 d to ensure neurotoxic concentration in hippocampus and hypothalamic region, part highly active in memory control and cognition. Neuroinflammation development was assessed by histological analyses and by investigating associated indices [β-secretase (BACE1), amyloid protein precursor (APP), presenilin (PSEN-1), and PSEN-2)]. Furthermore we measured the expression profile of lethal-7 (let-7) miRNAs members a, b, c, e, and f, a highly abundant regulator of gene expression in the CNS. Protein and mRNA levels of neuroinflammation markers COX-2, BACE1, APP, and iNOS were also attenuated by combined therapy. On the other hand, assessment of the indicated five let-7 members, showed distinct expression profile pattern in the different groups. Let-7 a, b, and c disappeared in the induced group, an effect that was partially suppressed by co-addition of either Cur or Resv. Attention is also paid to mechanisms by which Cur & Resv affect neuronal survival/apoptosis and proliferation/differentiation balance, as well as synaptic plasticity; these data suggest that the combined treatment induced significantly the expression of the five members when compared to rats treated with Cur or Resv only as well as to self-recovery group. The present study clearly indicates the possible benefit from the synergistic effect of Cur-Resv combination as therapeutic agents for neuroinflammation and its associated disorders in counteracting the damage inflicted by Al on rat brain region.

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