**Abstract**

Multiple sclerosis (MS) is an autoimmune disease of central nervous system with inflammatory basis. Experimental autoimmune encephalomyelitis (EAE) is common animal model used in experiments the most for investigating the multiple sclerosis due to many similar aspects. Hemp seed oil possess potential anti-inflammatory properties. In our research we investigated and compared the effect of hemp seed oil containing natural cannabinoids and polyunsaturated fatty acids on expression of cannabinoid receptors (CB) 1 and 2. Female C57bl/6 mice in three groups (8 in each) randomly allocated as follows: non-EAE (A), EAE treated with hemp seed oil (B) and EAE control (C). After one week of acclimatization in circadian rhythmic standard experimental condition mice were immunized, save group A. The day before induction (day zero), ip administration of hemp seed oil initiated and continued for 28 days. Clinical score and weight was recorded by a blind expert through the study and analysed by SPSS and ML-win where P value <0.05 considered statistically significant. Findings demonstrated a significant difference in clinical scores in group B compared to C (p values < 0.001). Moreover, expression of both CB1 and CB2 promoted significantly in group B in comparison to C (all p values < 0.001). This increase in CB2 expression was statistically more significant than CB1 expression. Numerous immunoregulatory, anti-inflammatory and anti-oxidant properties of hemp seed oil appraised for its polyunsaturated and/or essential fatty acids, anti-oxidants, vitamins and cannabinoids containment. Here in, hemp seed oil diminished clinical debilities probably through reduction in inflammation as confirmed by disease score descend. Furthermore, activation of CB1 and CB2 expression suggest pivotal role of these receptors in disease control.

**Keywords:** Nutraceuticals, Hemp Seed Oil, Cannabinoid Receptors (CB1, CB2), Gene Expression, Experimental Autoimmune Encephalomyelitis (EAE), Multiple Sclerosis (MS)

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