Peertechz

Journal of Neurology, Neurological Science and Disorders
submitpaper@peertechz.com

JOURNAL OF Neurology, Neurological Science and Disorders
OPEN ACCESS JOURNAL

ISSN: 2641-2950 DOI: https://dx.doi.org/10.17352/jnnsd

Research Article

Short report of potential Myelinogenesis effects of taper up-off of opium tincture in rodent model of multiple sclerosis

Hossein Dezhakam[1,2], Ani Dezhakam[1,2], Amin Dezhakam[1,2], Shani Dezhakam[1,2] and Arvin Haghighatfard[1]*

[1]Khwarizmi Institute of Science and Technology, Qeshm Island, Hormozgan, Iran

[2]Congress 60 Non-governmental organization, Iran

Received: 17 January, 2024
Accepted: 12 April, 2024
Published: 13 April, 2024

***Corresponding author:** Arvin Haghighatfard, Khwarizmi Institute of Science and Technology, Qeshm Island, Hormozgan, Iran, E-mail: arvinland@yahoo.com

Keywords: Myelinogenesis; Opium tincture; Multiple sclerosis; Taper up-off

Copyright License: © 2024 Dezhakam H, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

https://www.neuroscigroup.us

Abstract

Multiple Sclerosis (MS) is one of the most common demyelinating autoimmune diseases that affects the central nervous system and is characterized by major immune-mediated myelin and axonal damage or axonal loss explicable to the absence of myelin sheaths. Here we present the early findings of the gene expression study of myelinogenesis-related genes of MS rat models which were treated with a novel protocol of taper up-off of opium tincture.

The study included normal Lewis rats, MS rat models by induction of experimental autoimmune encephalomyelitis (EAE) without treatment, and MS rat models with a novel protocol of taper up-off treatment of opium tincture called Dezhakam-step-time (DST) in different dosages. RNA was extracted and cDNA was synthesized from the spinal cord tissue. Gene expression analysis was conducted for eight genes as markers of myelinogenesis (*OLIG1, OLIG2, MBP, MYRF, PLP1, PMP22, EGF*, and *UGT8*) using the Real-time PCR.

All eight genes were down-regulated in EAE models vs. healthy controls and all eight genes were up-regulated after the taper up-off treatment of opium tincture. The most over-expression of myelinogenesis-related genes was revealed at higher dosages of opium tincture.

These are the early results of a gene expression study in a multiple sclerosis model treated with opium tincture. It seems that the opium tincture method may induce the activation of myelinogenesis in EAE models which could lead to a potential treatment for improvement of neural dysfunctions in MS patients.

Introduction

Multiple Sclerosis (MS) is an autoimmune and demyelinating disorder [1] with enigmatic and controversial pathogenesis. While the humoral immune system and B cells and their associated antibodies play an important role in the pathogenesis of MS, it is mainly a T-cell-mediated autoimmune disease [2]. The main symptoms of MS are related to major demyelination and axonal loss along with short-term loss of nerve conduction and circulating factors [3].

Destruction of myelin sheaths and the myelin-producing Oligodendrocytes (ODCs) along with the remyelination failure had been reported in MS [4]. It has been reported that Epidermal Growth Factor (EGF) and normal prions are significantly reduced in the Central Nervous System (CNS) in MS and EGF administration could prevent demyelination and inflammatory reactions. On the other hand, cobalamin levels decrease in the spinal cord of MS patients [5].

OLIG1 and *OLIG2* genes are the main members of the gene family that encodes basic helix-loop-helix transcription factors that are expressed in the spinal cord and developing and mature Central Nervous System (CNS). OLIG proteins regulate cellular specification and differentiation in CNS including the development of oligodendrocytes and neural cells, and astrocyte

Citation: Dezhakam H, Dezhakam A, Dezhakam A, Dezhakam S, Haghighatfard A. (2024) Short report of potential Myelinogenesis effects of taper up-off of opium tincture in rodent model of multiple sclerosis. J Neurol Neurol Sci Disord 10(1): 021-026. DOI: https://dx.doi.org/10.17352/jnnsd.000060

specification [6]. *OLIG1* is a central regulator of oligodendrocyte myelinogenesis and axonal recognition. *OLIG1* is involved in the transcription regulation of most important myelin-specific genes, including *MBP*, *PLP1*, and *MAG*, and down the regulation of the *GFAP* gene which is a major astrocyte-specific gene [7]. Lack of *the OLIG1* gene could cause downregulation of myelin-specific genes, and *OLIG1*-null mice models show general progressive axonal degeneration and gliosis [8]. *OLIG2* is also a transcription factor that activates the expression of myelin-associated genes in the oligodendrocyte-lineage cells which in turn will lead to myelination [9].

Ciliary Neurotrophic Factor (CNTF) plays a major role in induction of promyelinating mechanism [10]. CNTF is an important survival factor for oligodendrocytes which protects oligodendrocytes from several death signals [11], along with effects in the maturation of oligodendroglial progenitor cells to mature myelin-forming cells, and myelinogenesis [12].

Experimental Autoimmune Encephalomyelitis (EAE) is the most accepted animal model of MS that can be induced by inoculation of susceptible animals with a range of CNS antigens including Myelin-Oligodendrocyte Glycoprotein (MOG). EAE would cause infiltration of the spinal cord and nerve roots with inflammatory cells that in turn would lead to demyelination of axons and axonal damages [13] along with glutamate toxicity and dysregulation of ion channels including calcium channels [14].

Gene expression profiling conducted on EAEs induced with Myelin-Oligodendrocyte Glycoprotein (MOG) in the spinal cords in mice and rats showed suppression of mRNA level of cholesterol biosynthesis and upregulation of immune-related molecules, extracellular matrix and cell adhesion molecules [15,16].

The present study was carried out to evaluate the gene expression pattern alterations of the multiple sclerosis model of Lewis rat (MOG-EAE), treated with a novel protocol of taper up-off of opium tincture, to understand the potential effects of opium on Multiple sclerosis. This paper is a short report of the early results of the study which focuses on the expression level of melanogenesis-related genes in experiment and control groups.

Methods & materials

Animal modeling of multiple sclerosis by induction of Experimental Autoimmune Encephalomyelitis (EAE)

Rodents were kept in an animal laboratory with regulated 12-hour light/12-hour dark cycles, with a climate-controlled environment and pathogen-free polystyrene cages designed for standard access to rodent chow and water. Based on previous studies and standard animal modeling of Multiple sclerosis, Experimental Autoimmune Encephalomyelitis (EAE) as a model of autoimmune central nervous system diseases has been used for modeling of demyelinating Multiple Sclerosis (MS) via injection of myelin oligodendrocyte glycoprotein (MOG) (MOG92-106) [17]. EAE was induced in 11-week-old male and female Lewis rats by subcutaneous injection at the base of the tail of 50 µg recombinant MOG, using standard methods based on previous studies. Healthy unimmunized rats with matched age weight and gender were used as controls. The list and description of groups are shown in Table 1.

Treatment with taper up-off treatment of opium tincture

We developed a laboratory-designed method of taper up-off treatment called the Dezhakam-step-time (DST) method, which starts Opium tincture dosage intake from the lowest dose on the first day and the dose will increase with a 20 % rate (or 0.8 coefficient) for each oral feeding (two times per day), until 18 oral feeding (9 days). Then the dosage of feeding is reduced by the same 20% rate (or 0.8 coefficient) for the next 18 oral feeding (9 days). The Rats will take the same dosage in first time and last time of oral feeding. A list of groups and descriptions of each group are presented in Table 1. Four sets of dosages were used in four experiment groups. In the present study dose one protocol started with 2.35 mg/kg Force-feeding and increased with 0.8 coefficient until 65.58 mg/kg in 18th oral feeding time. Doses two, three, and four started at 3.52 mg/kg, 4.7 mg/kg, and 5.87 mg/kg respectively.

Scarification and tissue collection

All rats were sacrificed on the same day at the standard animal laboratory. A sixty-milliliter syringe with a large bore blunt-ended needle is used to excise the spinal cord from the spinal column. All euthanasia processes were monitored by the researchers until confirmation of euthanasia accomplishment. Housing and euthanasia procedures are conducted based on the ARRIVE55 Guidelines checklist and protocols of previous studies [18,19].

RNA extraction

Total RNA was extracted from tissues using an RNA Purification kit (GeneJET™ RNA Purification Kit#K0732, Thermo scientific - Fermentas, Latvia) as per the manufacturer instructions and treated with DNase Treatment & Removal Reagents (DNase I, RNase-free (#EN0521) Fermentas, Latvia), according to the manufacture protocol to total removal of all traces of genomic DNAs. Quantity of extracted RNAs assessed by

Table 1: Groups' demographic data.

Group name	Description	Number of sacrificed rats
G1	EAE model treated with dose 1 opium tincture	six female/six male
G2	EAE model treated with dose 2 opium tincture	six female/five male
G3	EAE model treated with dose 3 opium tincture	six female/six male
G4	EAE model treated with dose 4 opium tincture	six female/six male
Multiple sclerosis model (EAE)	EAE model with no treatment	five female/six male
Normal control	Healthy rats with no treatment	six female/six male
Sham	Normal rats with force-feeding of water	six female/five male

EAE: experimental autoimmune encephalomyelitis.

Citation: Dezhakam H, Dezhakam A, Dezhakam A, Dezhakam S, Haghighatfard A. (2024) Short report of potential Myelinogenesis effects of taper up-off of opium tincture in rodent model of multiple sclerosis. J Neurol Neurol Sci Disord 10(1): 021-026. DOI: https://dx.doi.org/10.17352/jnnsd.000060

Nanodrop-1000 equipment and of RNAs quality check carried out using the BioRad Experion automated gel electrophoresis system (BioRad Laboratories Inc.) All extracted samples were restored in freezer storage at -80°C before further procedures.

Synthesis of cDNA

Copied DNA synthesized using the transcription first strand cDNA Synthesis Kit (RevertAid Premium First Strand cDNA Synthesis Kit #K1652, Thermo Scientific -Fermentas, Latvia) based on previous studies and protocol of Thermo Scientific company.

Gene expression analysis

The expression level of targeted genes (gene list presented in Table 2) was evaluated by Quantitative Real-time PCR. In the beginning specific primers and probes had been designed using "GenScript Real-time PCR (TaqMan) Primer Design " software and checked by blasting on the NCBI website. The RNA samples of randomly chosen control rats used for serial dilutions (1: 4) of pooled cDNA aimed to draw the standard curves. The CFX96 Touch Real-Time PCR Detection System (BIO-RAD, California, United States) is used for Quantitative Real-Time PCR with the triplicate method. Having no signal in no-template control samples along with an R^2 value more than 0.99 in the standard curve were two quality-checking criteria of Real-Time PCR analysis. The PCR reaction efficacy was calculated using an online software called Lin-Reg PCR (Amsterdam, Netherlands). TaqMan® PCR Starter Kit, Thermo Scientific - Fermentas, Latvia) used for all samples. The glyceraldehyde-3-phosphate dehydrogenase (*GAPDH*) is used as a housekeeping gene for normalization. Ratio calculation carried out by Livak formula.

Statistical examinations

Statistical assessments were performed with version 25 of SPSS. Normal distribution evaluation of all variables tested with Kolmogorov-Smirnov exam. One-way ANOVA analysis was used for statistical differences in multiple group comparisons. RNA integrity number, cDNA synthesis quality, plates/runs of qPCR, and primers and probe efficiency were defined as covariates, and the persistence of the significant difference between groups was evaluated by ANCOVA to control any potential confusion. Multiple comparisons corrections calculated Bonferroni correction statistical exam. The descriptive data are expressed as mean ± SD.

Results

During the treatment period one female rat from G2, one male rat from the multiple sclerosis model (EAE), and one female rat from the Sham group died before the scarification day. RNA quality analysis showed all samples had RNA Quality Indicator (RQI) values higher than 9.5. Results of gene expression assessments and comparisons between groups in differentially expressed genes are presented in Table 3. All genes were down-regulated in EAE models and up-regulated after the treatment in all four experiment groups. The greatest increase in mRNA levels was seen in G3 and G4. No significant difference was detected in the expression level of genes between female and male rats in any group.

Discussion

The molecular pathways leading to disease severity progression and remyelination failure or success in MS remain largely unknown [20]. While the molecular mechanisms of myelinogenesis and myelin gene activation and inactivation are not completely clarified, finding a potential way to activating of melanogenesis in MS patients, could lead to a potential treatment for neural loss of functions in CNS.

Our early results showed, that several markers of myelination [21] are down-regulated in the spinal cord during EAE and significantly raised after the force-feeding of opium tincture. Some of these genes are related to each other in several signaling pathways and contribute to neuronal plasticity. Interestingly, our results on the up-regulation of myelinogenesis markers weren't gender dependent which may lead to a potentially applicable treatment for both genders in MS.

Opium usage could enhance the antioxidant capacity and reduce the inflammation in the CNS which can reduce the extent of damage in cerebral ischemia [22]. Opium contains about frothy alkaloids and more than seventy components including several sugars and organic acids [23]. Some opioid-based analgesics such as morphine are associated with immunosuppressive effects on innate immunity, whilst having diverse effects on adaptive immunity [24]. It seems that using the whole alkaloid content of opium in a special taper-up-off protocol may induce anti-inflammation effects which in turn could lead to the gradual reactivation of myelinogenesis that has been reduced dramatically during the MS symptoms

Table 2: List of studied genes.

Gene symbol	Entrez gene name	Function
Olig1	oligodendrocyte transcription factor 1	It is involved in neuron differentiation and regulation of transcription by RNA polymerase II.
Olig2	oligodendrocyte transcription factor 2	It is a major regulator of ventral neuroectodermal progenitor cell fate.
MBP	Myelin Basic Protein	It is a major constituent of the myelin sheath of oligodendrocytes in the nervous system.
Myrf	myelin regulatory factor	It affects myelin production and regulation of myelin gene expression
Plp1	proteolipid protein 1	This gene encodes a transmembrane proteolipid protein which is the component of myelin.
Pmp22	peripheral myelin protein 22	This gene encodes an integral membrane protein which is a main component of myelin in the peripheral nervous system.
EGF	epidermal growth factor	This gene encodes a member of the epidermal growth factor superfamily and plays a major role in the growth, proliferation, and differentiation of numerous cells.
UGT8	UDP glycosyltransferase 8	The protein encoded by this gene belongs to the UDP-glycosyltransferase family that is involved in the biosynthesis of the myelin membrane of the central and peripheral nervous systems.

Citation: Dezhakam H, Dezhakam A, Dezhakam A, Dezhakam S, Haghighatfard A. (2024) Short report of potential Myelinogenesis effects of taper up-off of opium tincture in rodent model of multiple sclerosis. J Neurol Neurol Sci Disord 10(1): 021-026. DOI: https://dx.doi.org/10.17352/jnnsd.000060

Table 3: mRNA level and statistical comparisons of gene expression evaluations.

Gene	G1	G2	G3	G4	MS model	Sham
Olig1	Ratio: 0.61 P value:0.008	Ratio: 0.66 P value:0.01	Ratio: 0.78 P value:0.08	Ratio: 0.83 P value:0.19	Ratio: 0.51 P value:0.006	Ratio: 0.94 P value:0.28
Olig2	Ratio: 0.69 P value:0.008	Ratio: 0.73 P value:0.01	Ratio: 0.82 P value:0.07	Ratio: 0.86 P value:0.12	Ratio: 0.42 P value:0.001	Ratio: 0.91 P value:0.77
MBP	Ratio: 0.73 P value:0.006	Ratio: 0.78 P value:0.01	Ratio: 0.88 P value:0.1	Ratio: 0.85 P value:0.13	Ratio: 0.67 P value:0.004	Ratio: 0.96 P value:0.35
Myrf	Ratio: 0.68 P value:0.006	Ratio: 0.75 P value:0.01	Ratio: 0.91 P value:0.15	Ratio: 0.93 P value:0.21	Ratio: 0.59 P value:0.004	Ratio: 0.96 P value:0.68
Plp1	Ratio:0.59 P value:0.008	Ratio:0.64 P value:0.009	Ratio:0.83 P value:0.07	Ratio: 0.94 P value:0.1	Ratio: 0.48 P value:0.002	Ratio: 1.06 P value:0.29
Pmp22	Ratio:0.7 P value:0.01	Ratio:0.77 P value:0.03	Ratio:0.84 P value:0.12	Ratio: 0.9 P value:0.17	Ratio: 0.53 P value:0.004	Ratio: 0.9 P value:0.47
EGF	Ratio: 0.77 P value:0.06	Ratio: 0.83 P value:0.09	Ratio: 0.82 P value:0.11	Ratio:88 P value:0.15	Ratio: 0.71 P value:0.006	Ratio: 0.92 P value:0.3
UGT8	Ratio: 0.73 P value:0.009	Ratio: 0.78 P value:0.01	Ratio: 0.84 P value:0.04	Ratio:92 P value:0.08	Ratio:0.62 P value:0.005	Ratio: 1.1 P value:0.2

MS: multiple sclerosis, *OLIG1*: oligodendrocyte transcription factor 1, *OLIG2*: oligodendrocyte transcription factor 2, *MBP*: myelin basic protein, *MYRF*: myelin regulatory factor, *PLP1*: proteolipid protein 1, *PMP22*: peripheral myelin protein 22, *EGF*: epidermal growth factor, *UGT8*: UDP glycosyltransferase 8.

advancement. The mechanism and mode of action of the DST method at the molecular level are not completely clarified, but it seems that opium, with several alkaloids, can help regulate upstream mechanisms of gene expression and epigenetics, especially transcription factors.

Previous studies showed the myelination expression patterns alterations in the spinal cords of EAE mice models induced by estrogen [25]. It has been suggested that signaling pathways that promote myelin formation and repair could enhance remyelination [20]. To the best of our knowledge, the main reasons for remyelination failure in EAE models as well as human MS patients include calpain genes overexpression and activation of glycolipid-reactive iNKT cells and sphingoid-mediated inflammation. In addition, the treatments for MS patients are based on Cytokine-based immune intervention, antigen-based immunomodulation, and also recombinant monoclonal antibodies which induce remyelination.

Major attribution of EGF in myelin gene expression, myelin sheath compaction, and myelinogenesis had been reported in both peripheral and central nervous systems [26]. Although the processes of molecular mechanisms underlying oligodendrocyte myelinogenesis are poorly defined the significant over-expression of OLIG genes is a reliable marker for myelinogenesis activation [27]. Moreover, *MYRF* is required to initiate and maintain myelination, and upregulation of *MYRF* along with *MBP*, *UGT8*, *PLP1*, and *PMP22* could orchestrate the remyelination in neurodegenerative disease which in turn may lead to the improvement of the circuit's functions in CNS [28]. The neural circuit's normal functions need several types of neurons astrocytes and oligodendrocytes, at the appropriate periods and regions [29].

Multiple sclerosis (MS) management mostly aims to control acute attacks and manage progressive worsening, and disabling symptoms [30]. Several classes of disease-modifying therapies (DMTs), with different target mechanisms of action and administration protocol, are available for MS patients that aim to control the relapsing, prevention from neurological disability, and progression of ongoing inflammatory activity. The list of these drugs included but not limited to interferons, glatiramer acetate, sphingosine 1-phosphate receptor modulators, cladribine, and three types of monoclonal antibodies. Most recently for patients with primary progressive MS, the ocrelizumab has been approved and added to the list worldwide [31]. All of these treatments are focused on the immune system and control of neurological disabilities. Results of the present short report present the potential effect of a novel protocol opium tincture to regenerate the myelin and restore lost neurological capabilities.

Limitations

Multiple Sclerosis (MS) is an inflammatory and demyelinating disease of the Central Nervous System (CNS) that results in variable severities of neurodegeneration. While the early results of the present study were interesting, the myelination is not universally applied in the central nervous system and may vary in the spinal cord versus the brain in EAE models. Further results especially the whole genome expression profiling of samples may clarify our knowledge about the effects of opium usage with the DST method on the EAE model.

Conclusion

Our early results showed a significant gene expression alteration in myelinogenesis-related genes which may lead to the development of a treatment strategy that induces myelination and restoring of affected neurons in CNS. Altering the epigenetic pattern of related genes; may apply to other severe neurodegenerative diseases with loss of the neuronal circuits such as Huntington's Disease (HD), Parkinson's Disease (PD), and Amyotrophic Lateral Sclerosis (ALS) as well as MS. Therefore, the DST method of taper up-off of opium could improve the speed and efficiency of signal propagation. While myelinogenesis is a complex process in oligodendrocytes functions, glial process, and axon spiraling, and the nature of the opium tincture effects on this process still needs to be clarified, current results may increase the hopes for a new treatment to

Citation: Dezhakam H, Dezhakam A, Dezhakam A, Dezhakam S, Haghighatfard A. (2024) Short report of potential Myelinogenesis effects of taper up-off of opium tincture in rodent model of multiple sclerosis. J Neurol Neurol Sci Disord 10(1): 021-026. DOI: https://dx.doi.org/10.17352/jnnsd.000060

improve multiple sclerosis as well as demyelination in other disorders.

Ethics statement

This research was approved by the Central Ethical Committee of the Islamic Azad University with the approval number 38966. All animal modeling processes and experiments are conducted based on ARRIVE (Animal Research: Reporting of in Vivo Experiments) guidelines 2.0 and under ethical committee supervision.

References

1. Pahan K. Neuroimmune pharmacological control of EAE. J Neuroimmune Pharmacol. 2010 Jun;5(2):165-7. doi: 10.1007/s11481-010-9219-6. Epub 2010 Apr 23. PMID: 20414732; PMCID: PMC2881219.
2. Wilson HL. B cells contribute to MS pathogenesis through antibody-dependent and antibody-independent mechanisms. Biologics. 2012; 6:117-23. doi: 10.2147/BTT.S24734. Epub 2012 May 7. PMID: 22690126; PMCID: PMC3363029.
3. Schneider C, Schuetz G, Zollner TM. Acute neuroinflammation in Lewis rats - a model for acute multiple sclerosis relapses. J Neuroimmunol. 2009 Aug 18;213(1-2):84-90. doi: 10.1016/j.jneuroim.2009.05.015. Epub 2009 Jun 26. PMID: 19560215.
4. Scalabrino G. Epidermal Growth Factor in the CNS: A Beguiling Journey from Integrated Cell Biology to Multiple Sclerosis. An Extensive Translational Overview. Cell Mol Neurobiol. 2022 May;42(4):891-916. doi: 10.1007/s10571-020-00989-x. Epub 2020 Nov 5. PMID: 33151415; PMCID: PMC8942922.
5. Scalabrino G. New Epidermal-Growth-Factor-Related Insights In to the Pathogenesis of Multiple Sclerosis: Is It Also Epistemology? Front Neurol. 2021 Nov 26; 12:754270. doi: 10.3389/fneur.2021.754270. PMID: 34899572; PMCID: PMC8664554.
6. Szu JI, Tsigelny IF, Wojcinski A, Kesari S. Biological functions of the Olig gene family in brain cancer and therapeutic targeting. Front Neurosci. 2023 May 18; 17:1129434. doi: 10.3389/fnins.2023.1129434. PMID: 37274223; PMCID: PMC10232966.
7. Zhang Y, Chen K, Sloan SA, Bennett ML, Scholze AR, O'Keeffe S, Phatnani HP, Guarnieri P, Caneda C, Ruderisch N, Deng S, Liddelow SA, Zhang C, Daneman R, Maniatis T, Barres BA, Wu JQ. An RNA-sequencing transcriptome and splicing database of glia, neurons, and vascular cells of the cerebral cortex. J Neurosci. 2014 Sep 3;34(36):11929-47. doi: 10.1523/JNEUROSCI.1860-14.2014. Erratum in: J Neurosci. 2015 Jan 14;35(2):846-6. PMID: 25186741; PMCID: PMC4152602.
8. Xin M, Yue T, Ma Z, Wu FF, Gow A, Lu QR. Myelinogenesis and axonal recognition by oligodendrocytes in brain are uncoupled in Olig1-null mice. J Neurosci. 2005 Feb 9;25(6):1354-65. doi: 10.1523/JNEUROSCI.3034-04.2005. PMID: 15703389; PMCID: PMC6725991.
9. Zhang K, Chen S, Yang Q, Guo S, Chen Q, Liu Z, Li L, Jiang M, Li H, Hu J, Pan X, Deng W, Xiao N, Wang B, Wang ZX, Zhang L, Mo W. The Oligodendrocyte Transcription Factor 2 OLIG2 regulates transcriptional repression during myelinogenesis in rodents. Nat Commun. 2022 Mar 17;13(1):1423. doi: 10.1038/s41467-022-29068-z. Erratum in: Nat Commun. 2022 Jun 1;13(1):3164. PMID: 35301318; PMCID: PMC8931116.
10. Stankoff B, Aigrot MS, Noël F, Wattilliaux A, Zalc B, Lubetzki C. Ciliary neurotrophic factor (CNTF) enhances myelin formation: a novel role for CNTF and CNTF-related molecules. J Neurosci. 2002 Nov 1;22(21):9221-7. doi: 10.1523/JNEUROSCI.22-21-09221.2002. PMID: 12417647; PMCID: PMC6758026.
11. Louis JC, Magal E, Takayama S, Varon S. CNTF protection of oligodendrocytes against natural and tumor necrosis factor-induced death. Science. 1993 Jan 29;259(5095):689-92. doi: 10.1126/science.8430320. PMID: 8430320.
12. Barres BA, Schmid R, Sendnter M, Raff MC. Multiple extracellular signals are required for long-term oligodendrocyte survival. Development. 1993 May;118(1):283-95. doi: 10.1242/dev.118.1.283. PMID: 8375338.
13. Herz J, Zipp F, Siffrin V. Neurodegeneration in autoimmune CNS inflammation. Exp Neurol. 2010 Sep;225(1):9-17. doi: 10.1016/j.expneurol.2009.11.019. Epub 2009 Dec 1. PMID: 19961850.
14. Ohgoh M, Hanada T, Smith T, Hashimoto T, Ueno M, Yamanishi Y, Watanabe M, Nishizawa Y. Altered expression of glutamate transporters in experimental autoimmune encephalomyelitis. J Neuroimmunol. 2002 Apr;125(1-2):170-8. doi: 10.1016/s0165-5728(02)00029-2. PMID: 11960654.
15. Ibrahim SM, Mix E, Böttcher T, Koczan D, Gold R, Rolfs A, Thiesen HJ. Gene expression profiling of the nervous system in murine experimental autoimmune encephalomyelitis. Brain. 2001 Oct;124(Pt 10):1927-38. doi: 10.1093/brain/124.10.1927. PMID: 11571211.
16. Mueller AM, Pedré X, Stempfl T, Kleiter I, Couillard-Despres S, Aigner L, Giegerich G, Steinbrecher A. Novel role for SLPI in MOG-induced EAE revealed by spinal cord expression analysis. J Neuroinflammation. 2008 May 26;5:20. doi: 10.1186/1742-2094-5-20. PMID: 18501024; PMCID: PMC2438345.
17. Miller SD, Karpus WJ, Davidson TS. Experimental autoimmune encephalomyelitis in the mouse. Curr Protoc Immunol. 2010 Feb;Chapter 15:15.1.1-15.1.20. doi: 10.1002/0471142735.im1501s88. PMID: 20143314.
18. Inglis HR, Greer JM, McCombe PA. Gene expression in the spinal cord in female lewis rats with experimental autoimmune encephalomyelitis induced with myelin basic protein. PLoS One. 2012;7(11):e48555. doi: 10.1371/journal.pone.0048555. Epub 2012 Nov 6. PMID: 23139791; PMCID: PMC3491034.
19. Shomer NH, Allen-Worthington KH, Hickman DL, Jonnalagadda M, Newsome JT, Slate AR, Valentine H, Williams AM, Wilkinson M. Review of Rodent Euthanasia Methods. J Am Assoc Lab Anim Sci. 2020 May 1;59(3):242-253. doi: 10.30802/AALAS-JAALAS-19-000084. Epub 2020 Mar 5. PMID: 32138808; PMCID: PMC7210730.
20. El Behi M, Sanson C, Bachelin C, Guillot-Noël L, Fransson J, Stankoff B, Maillart E, Sarrazin N, Guillemot V, Abdi H, Cournu-Rebeix I, Fontaine B, Zujovic V. Adaptive human immunity drives remyelination in a mouse model of demyelination. Brain. 2017 Apr 1;140(4):967-980. doi: 10.1093/brain/awx008. PMID: 28334918; PMCID: PMC5382952.
21. Massella A, D'Intino G, Fernández M, Sivilia S, Lorenzini L, Giatti S, Melcangi RC, Calzà L, Giardino L. Gender effect on neurodegeneration and myelin markers in an animal model for multiple sclerosis. BMC Neurosci. 2012 Jan 24; 13:12. doi: 10.1186/1471-2202-13-12. PMID: 22272832; PMCID: PMC3282645.
22. Yarahmadzehi S, Fanaei H, Mirshekar MA, Atashpanjeh AR. Opium consumption exerts protective effect against cerebral ischemia by reducing inflammation and enhancing antioxidant defense in male rats. Neurology, Psychiatry and Brain Research. 2020 Sep 1; 37:15-20.
23. Shetge SA, Dzakovich MP, Cooperstone JL, Kleinmeier D, Redan BW. Concentrations of the Opium Alkaloids Morphine, Codeine, and Thebaine in Poppy Seeds are Reduced after Thermal and Washing Treatments but are Not Affected when Incorporated in a Model Baked Product. J Agric Food Chem. 2020 May 6;68(18):5241-5248. doi: 10.1021/acs.jafc.0c01681. Epub 2020 Apr 27. PMID: 32302121; PMCID: PMC9087216.
24. Abdel Shaheed C, Beardsley J, Day RO, McLachlan AJ. Immunomodulatory effects of pharmaceutical opioids and antipyretic analgesics: Mechanisms and relevance to infection. Br J Clin Pharmacol. 2022 Jul;88(7):3114-3131. doi: 10.1111/bcp.15281. Epub 2022 Mar 1. PMID: 35229890.
25. Matejuk A, Dwyer J, Hopke C, Vandenbark AA, Offner H. 17Beta-estradiol treatment profoundly down-regulates gene expression in spinal cord tissue in mice protected from experimental autoimmune encephalomyelitis. Arch Immunol Ther Exp (Warsz). 2003;51(3):185-93. PMID: 12894873.
26. Tawk M, Makoukji J, Belle M, Fonte C, Trousson A, Hawkins T, Li H, Ghandour S, Schumacher M, Massaad C. Wnt/beta-catenin signaling is an essential and direct driver of myelin gene expression and myelinogenesis. J Neurosci. 2011 Mar 9;31(10):3729-42. doi: 10.1523/JNEUROSCI.4270-10.2011. PMID: 21389228; PMCID: PMC6622795.

Citation: Dezhakam H, Dezhakam A, Dezhakam A, Dezhakam S, Haghighatfard A. (2024) Short report of potential Myelinogenesis effects of taper up-off of opium tincture in rodent model of multiple sclerosis. J Neurol Neurol Sci Disord 10(1): 021-026. DOI: https://dx.doi.org/10.17352/jnnsd.000060

27. Lee DG, Kim YK, Baek KH. The bHLH Transcription Factors in Neural Development and Therapeutic Applications for Neurodegenerative Diseases. Int J Mol Sci. 2022 Nov 11;23(22):13936. doi: 10.3390/ijms232213936. PMID: 36430421; PMCID: PMC9696289.

28. Wang S, Wang Y, Zou S. A Glance at the Molecules That Regulate Oligodendrocyte Myelination. Curr Issues Mol Biol. 2022 May 15;44(5):2194-2216. doi: 10.3390/cimb44050149. PMID: 35678678; PMCID: PMC9164040.

29. Xin W, Chan JR. Myelin plasticity: sculpting circuits in learning and memory. Nat Rev Neurosci. 2020 Dec;21(12):682-694. doi: 10.1038/s41583-020-00379-8. Epub 2020 Oct 12. PMID: 33046886; PMCID: PMC8018611.

30. Hauser SL, Cree BAC. Treatment of Multiple Sclerosis: A Review. Am J Med. 2020 Dec;133(12):1380-1390.e2. doi: 10.1016/j.amjmed.2020.05.049. Epub 2020 Jul 17. PMID: 32682869; PMCID: PMC7704606.

31. McGinley MP, Goldschmidt CH, Rae-Grant AD. Diagnosis and Treatment of Multiple Sclerosis: A Review. JAMA. 2021 Feb 23;325(8):765-779. doi: 10.1001/jama.2020.26858. Erratum in: JAMA. 2021 Jun 1;325(21):2211. PMID: 33620411.

Discover a bigger Impact and Visibility of your article publication with Peertechz Publications

Highlights

- Signatory publisher of ORCID
- Signatory Publisher of DORA (San Francisco Declaration on Research Assessment)
- Articles archived in worlds' renowned service providers such as Portico, CNKI, AGRIS, TDNet, Base (Bielefeld University Library), CrossRef, Scilit, J-Gate etc.
- Journals indexed in ICMJE, SHERPA/ROMEO, Google Scholar etc.
- OAI-PMH (Open Archives Initiative Protocol for Metadata Harvesting)
- Dedicated Editorial Board for every journal
- Accurate and rapid peer-review process
- Increased citations of published articles through promotions
- Reduced timeline for article publication

Submit your articles and experience a new surge in publication services
https://www.peertechzpublications.org/submission

Peertechz journals wishes everlasting success in your every endeavours.

Citation: Dezhakam H, Dezhakam A, Dezhakam A, Dezhakam S, Haghighatfard A. (2024) Short report of potential Myelinogenesis effects of taper up-off of opium tincture in rodent model of multiple sclerosis. J Neurol Neurol Sci Disord 10(1): 021-026. DOI: https://dx.doi.org/10.17352/jnnsd.000060