Review Form 1.6

Journal Name:	**Journal of Pharmaceutical Research International**
Manuscript Number:	**Ms_JPRI_93538**
Title of the Manuscript:	**Gene therapies for Spinal muscular atrophy and Duchenne muscular dystrophy : a pathbreaking moment in therapeutics**
Type of the Article	**Review Article**

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty'**, provided the manuscript is scientifically robust and technically sound.
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PART 1: Review Comments

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Compulsory REVISION comments		
Minor REVISION comments	**The manuscript is dealing with a novel topic which is very interesting , the manuscript is well presented to the main idea although it requires some minor modifications be ALL performed before publication as follows;** **1-The abstract better to be divided as Background, Aim, Method, Result and discussion rather being one whole piece.** **2-The quality of resolution if both figures 2 and 3 is poor. Please upgrade their quality of resolution.** **3- Figure captions required to be written in more details explaining each the three figures in a more comprehensive form under the figure title.** **4- *The authors SHOULD add the following paragraph at the introduction of the review as different types of supplemental treatment as neuroprotective used for neuropathy accompanied with many diseases and which could be compared with gene therapy the main of their review;*** Prepulse inhibition (PPI) of startle response is a valuable paradigm for sensorimotor gating processes, thus, the effects of administration of the anti-amnestic dose of the extract and hyperforin were tested on PPI of an acoustic startle response in rats. The exacerbating effect of St. John's wort extract on PPI deficit may provide a limitation for using the extract to manage cognitive disturbance in psychotic and Huntington's disease patients manifesting PPI deficit.(1) Additionally, serotoninergic 5-HT1A and 5-HT2A, alpha-adrenergic and dopaminergic D1 receptors are involved in the disruptive effect of St. John's wort extract on PPI response in rats. We can also conclude that hyperforin, and not hypericin, is one of the active ingredients responsible for St. John's wort-induced PPI disruption with no relation to apoptotic processes.(2) It is worthy to mention that, coenzyme Q10 and alpha-tocopherol which have a neuroprotective, proved to have protective effects of antioxidants (3). Besides, vitamin D is one of essential vitamins was not only deficient in autistism but also contribute to pathogenesis of the disease in these patients (4). Moreover, estrogenic compounds as genistein proved to exhibit a neuroprotective effect attributed to its estrogenic, antioxidant, and/or anti-apoptotic properties (5). Diabetic Polyneuropathy (DPN) represents a major health problem as it increases morbidity affecting patients' quality of life. Vitamin B frequently is used for treating DPN. ALPHA Lipoic Acid (ALA) seems to delay or reverse DPN Combined therapy of DPN with ALA and Vitamin B complex, orally for 12 weeks improves the symptoms of neuropathy evidenced by using Michigan Neuropathy Screening Instrument (MNSI) questionnaire same as in Nerve Conduction Studies (NCS).(6) Paclitaxel-induced peripheral neuropathy (PIPN) is a common adverse event that occurs with paclitaxel therapy and frequently causes neuropathy, considerable pain and a decline in patients' quality of life. Single nucleotide polymorphisms (SNPs) in the ABCB1 gene have been frequently associated with increased severity of PIPN. The ABCB1 G1236A, BSA, and history of diabetes are valid predictors of PIPN, which can enable the personalization of paclitaxel dosing to prevent PIPN.(7) **References** **(1) Mariane G. Tadros, Mohamed R. Mohamed, Amal M. Youssef, Gilane M. Sabry, Nagwa A. Sabry, Amani E. Khalifa. Proapoptotic and prepulse inhibition (PPI) disrupting effects of Hypericum perforatum in rats. Journal of Ethnopharmacology 122 (2009) 561–566. https://doi.org/10.1016/j.jep.2009.01.009.** **(2) Mariane G. Tadros , Mohamed R. Mohamed , Amal M. Youssef , Gilane M. Sabry, Nagwa A. Sabry, Amani E. Khalifaa Involvement of serotoninergic 5-HT1A/2A, alpha-adrenergic and dopaminergic D1 receptors in St. John's wort-induced prepulse inhibition deficit: A possible role of hyperforin.**	

	Behavioural Brain Research 199 (2009) 334–339. doi:10.1016/j.bbr.2008.12.015 **(3) Marwa M Nagib, Mariane G Tadros, Hadwa Ali Abd Al-khalek, Rania M Rahmo, Nagwa Ali Sabri, Amani E Khalifa, Somaia I Masoud. Molecular mechanisms of neuroprotective effect of adjuvant therapy with phenytoin in pentylenetetrazole-induced seizures: Impact on Sirt1/NRF2 signaling pathways. Neurotoxicology Vol. 68, 47-65, 2018. https://doi.org/10.1016/j.neuro.2018.07.006.** **(4) S. F. Fahmy, N. A. Sabri, M. H. El Hamamsy, M. El Sawi, O. K. Zak. Vitamin D Intake and Sun Exposure in Autistic Children. JPSR, 2016; Vol. 7(3): 1043-1049. DOI: 10.13040/IJPSR.0975-8232.7(3).1043-49.** **(5) Amr A. Elsayed , Esther T. Menze, Mariane G. Tadros, Bassant M. M. Ibrahim, Nagwa A. Sabri , Amani E. Khalifa. Naunyn-Schmiedeberg's Arch Pharmacol (2018). Effects of genistein on pentylenetetrazole-induced behavioral and neurochemical deficits in ovariectomized rats 391:27–36 https://doi.org/10.1007/s00210-017-1435-7.** **(6) Boghdadi MA, Afify HE , Sabri N , Makboul K and Elmazar M. Comparative Study of Vitamin B Complex Combined with Alpha Lipoic Acid versus Vitamin B Complex in Treatment of Diabetic Polyneuropathy in Type 2 Diabetic Patients. Clin Exp Pharmacol 2017, 7:4 DOI: 10.4172/2161-1459.1000241.** **(7) Nabil M. Abdelfattah, Mohamed H. Solayman, Yasser Elnahass , and Nagwa A. Sabri. ABCB1 Single Nucleotide Polymorphism Genotypes as Predictors of Paclitaxel-Induced Peripheral Neuropathy in Breast Cancer. GENETIC TESTING AND MOLECULAR BIOMARKERS ,Volume 25, Number 7, 2021, Mary Ann Liebert, Inc. Pp. 471–477 DOI: 10.1089/gtmb.2021.001** 5- The authors SHOULD divide the review into sections including; Introduction (which is present and to contain several treatment methods for the topic disease), Method (collection of review data as websites, links…..), Results and Discussion (including the researches with their results which was already presented by the authors in the review), and Conclusion. 6- The authors better to mention the side effects and adverse events of each gene therapy in the review so as to have a full image about each medication. 7- Pathophysiology, signs and symptoms as well as diagnosis of the Spinal muscular atrophy and Duchenne muscular dystrophy to be written briefly in the review.	
Optional/General comments		

PART 2:

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	

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