USING THE NATURAL ECO-FRIENDLY PHYTOCHEMICAL, METHYL DIHYDROJASMONATE, FOR MANAGEMENT OF HUNTINGTON'S DISEASE. (S-02)

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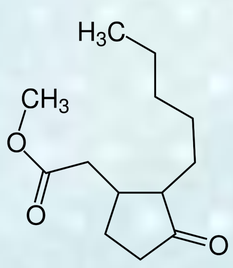
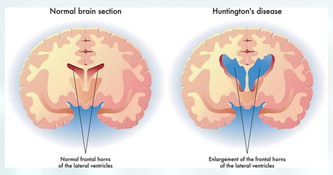
Introduction

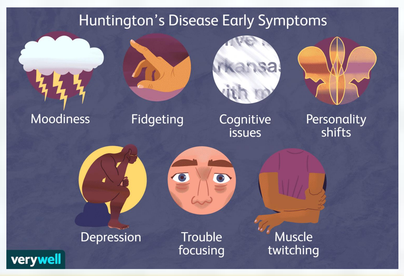
Huntington's disease (HD) is an inherited debilitating neurodegenerative disease with a very detrimental influence on the health and productivity of patients. It develops between 35 to 45 years. The characteristic degeneration of striatal medium spiny neurons of the basal ganglia is responsible for the motor, cognitive, and behavioral abnormalities associated with the disease. Psychiatric disturbances, apathy and psychosocial problems as obsessive-compulsive behavior, aggression and psychosis are very common in HD patients.

Chemotherapy often results in serious side effects that limit the dose administered to patients, due to its non-specific action on both cancerous and healthy cells, leading to a compromised immune system.

Methyl dihydrojasmonate (MDHJ) is a recently reported selective anticancer derivative of jasmonates; a class of plant stress hormones produced from Jasmine plant (Jasminum officinale). Upon wounding or pathogenic attack, MDHJ causes induction and accumulation of proteinase inhibitors which are involved in the activation of programmed cell death resembling mammalian apoptosis. MDHJ is reportedly used for the management of HD owing to its action via modulation of the antioxidant defense, inflammatory biomarkers, neurotransmitter regulation, and neuronal regeneration. In addition to its safety profile and limited toxicity in normal cells.







Objective

The main objective of the current study is the preparation and characterization of novel lipid based nano delivery system of the herbal drug (MDHJ) for the management of Huntington's disease.

Methodology and Results

1-Preparation of MDHJ loaded formulations :

Nanostructured lipid carriers loaded with MDHJ were prepared by hot homogenization method using the lipid carrier Gelucire 50/13 in addition to the liquid lipid Miglyol together with Precirol in order to achieve maximum drug entrapment coupled with stability (Table 1).

Table 1 : Composition of prepared NLC formulations; blank and loaded with MDHJ

Concentration (%W/V)				
Formula code	Lipid		Stabilizer	Drug
	Gelucire 50/13	Miglyol	Precirol	MDHJ
Blank	1	1	1	0
Formula A1				1

2-Charaterization of the prepared formulation:

TEM, colloidal properties and pharmaceutical performance indicators were assessed for the selected formulations including particle size, zeta potential, in-vitro release and stability at room temperature for 6 months.

A-Transmission electron microscopy.

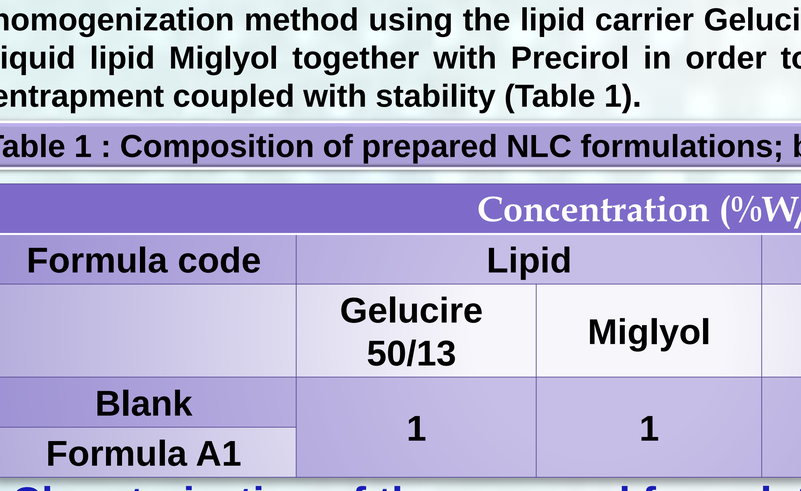


Fig.1: TEM micrographs of NLC loaded formulation

The Particle morphological characterization of prepared formulations was investigated with Transmission electron microscopy (TEM) using a negative-staining method. The TEM micrographs of the selected MDHJ- SLNs formulations (Fig.1) revealed that G 50/13-based NLCs showed an optimum size range compared which also came in accordance with particle size measurements. The formulations show phase contrast revealing the incorporation of MDHJ in the NLC core

B-Determination of colloidal properties

The prepared MDHJ-NLC formulation showed good quality attributes including; particle size, PDI values and zeta potential (Table 2).

Formula code	PS (nm) ± SD	PDI± SD	ZP (mv) ± SD
A1	149.8 ±0.532	0.280 ± 0.006	-13.3 ± 0.056

Table 2: Colloidal properties of Selected MDHJ-SLN formulations

C- In-vitro drug release

The tested formulation showed biphasic release profile suitable for treatment compared to the MDHJ true solution.

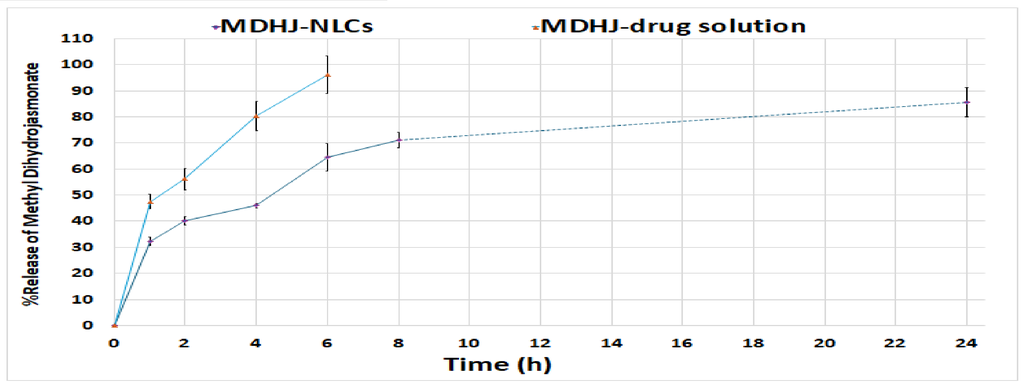


Fig. 2: In-vitro release profile of MDHJ loaded formulation

D-Shelf stability study

The formulation showed a short-term/good stability at room temperature for 6 months study.

Fig 3: In-vitro release profiles of MDHJ loaded formulation freshly prepared and after 3 and 6 months on the shelf.

E-*In-vivo* assessment of HD progression

HD was induced in male Sprague Dawley rats by injection of 3-nitropropionic acid (3-NP; 10 mg/kg) for 14 days. Rats were then divided into 5 groups of normal control (CN), positive control (HD), treated with MDHJ, or MDHJ-NLC or NLC. Drugs were given daily for 21 days. Assessment of HD progression was done using HD score (0=normal behaviour; 1= general slowness; 2= prominent gait abnormality with poor coordination; 3= nearly complete hind-limb paralysis; 4=inability to move; and 5= recumbency or death) and the behavioural studies: rotarod, open field and Y-Maze (Fig.4).

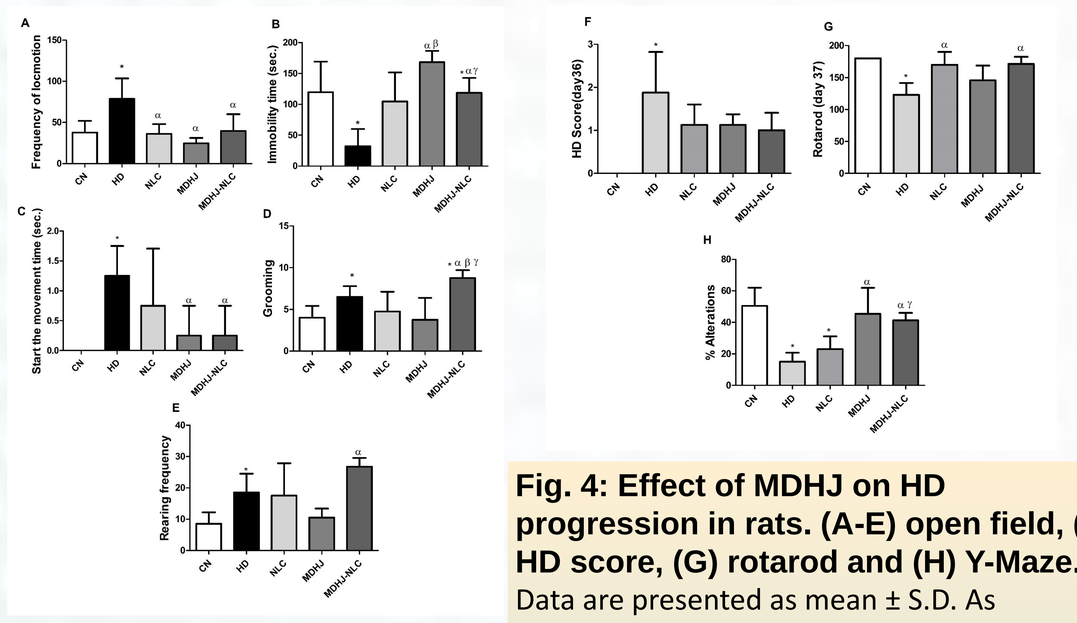


Fig. 4: Effect of MDHJ on HD progression in rats. (A-E) open field, (F) HD score, (G) rotarod and (H) Y-Maze. Data are presented as mean ± S.D. As compared with (*) CN, (α) HD, (β) NLC and (ɣ) MDHJ at $p<0.05$.

Conclusion

Performed tests showed the ability to incorporate the natural plant hormone MDHJ successfully in a stable nano formulation having optimum colloidal properties. In-*vivo*, MDHJ-NLC was able to improve the HD score and most studies behavioural changes associated with the disease.

References

1-Gupta, Swati, and Manish K. Gupta. "Possible role of nanocarriers in drug delivery against cervical cancer." *Nano reviews & experiments. 2017;* 8.1: 1335567.

2- da Silva, Gisela Bevilacqua Rolfsen Ferreira, et al. "An analytical GC-MS method to quantify methyl dihydrojasmonate in biocompatible oil-in-water microemulsions: physicochemical characterization and in vitro release studies." *Pharmaceutical development and technology. 2018;* 23.2: 151-157.