Evaluation of the anti-inflammatory response of Angiotensin 1-7 associated with liposomes administered via inhalation in mice with experimental autoimmune encephalomyelitis

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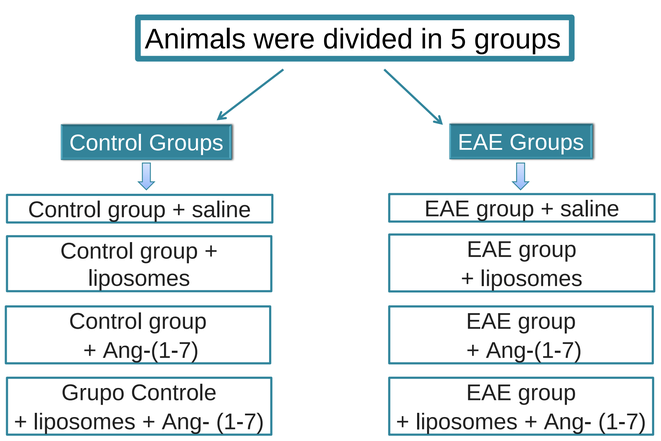
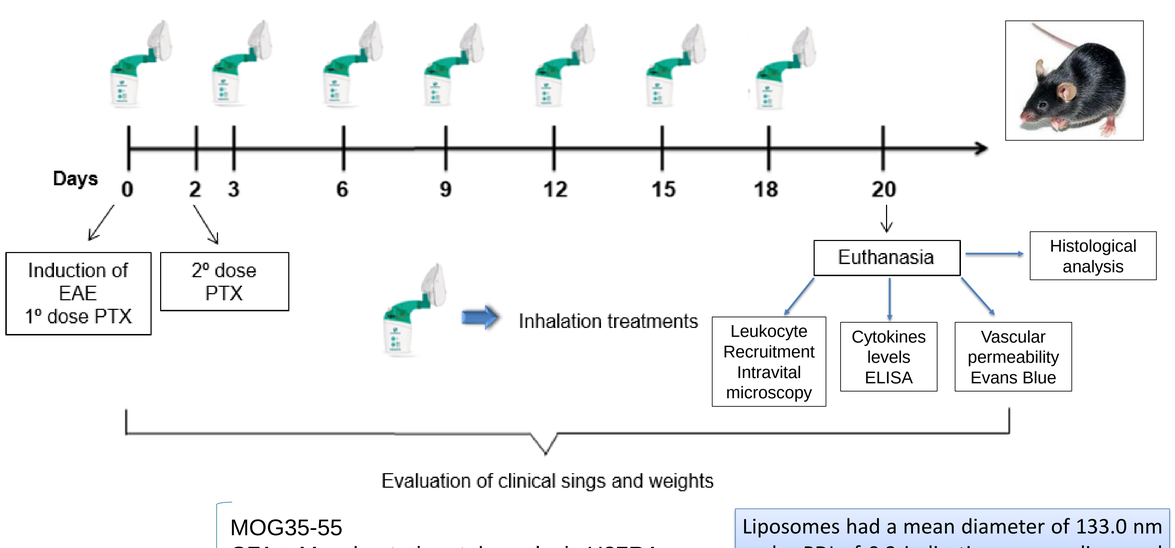
INTRODUCTION

Multiple sclerosis is a chronic, progressive and autoimmune disease characterized by inflammatory infiltrates, gliosis, demyelination and axonal degeneration in the central nervous system. Currently used therapies are generally associated with inconvenient methods of administration and severe side effects impairing patient safety and adherence to therapy.

So, the objective of this research was evaluate the anti-inflammatory response of encapsulated-Ang-(1-7) in liposomes inhaled by mice with experimental autoimmune encephalomyelitis.



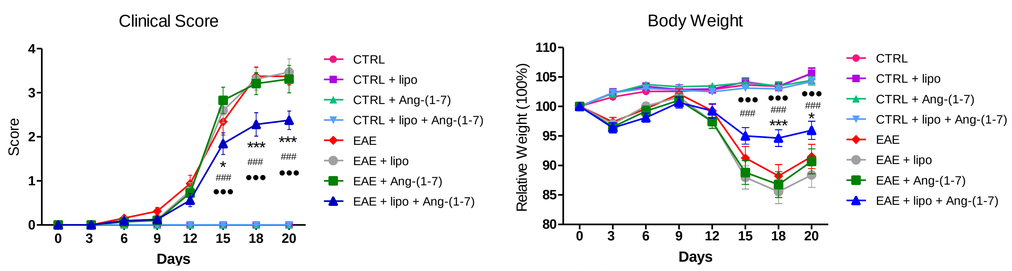
Clinical signs	Score
No clinical signs	0
Partially limp tail	1
Paralyzed tail	2
Hind limb paresis, uncoordinated movement	3
One hind limb paralyzed	4
Both hind limbs paralyzed	5
Hind limbs paralyzed, weakness in forelimbs	6
Hind limbs paralyzed, one forelimb paralyzed	7
Hind limbs paralyzed, both forelimbs paralyzed	8
Moribund	9
Death	10

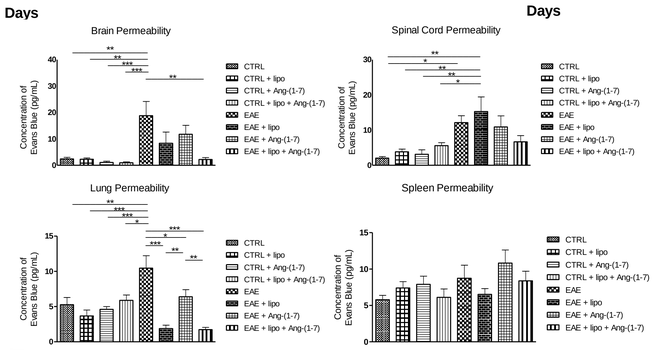


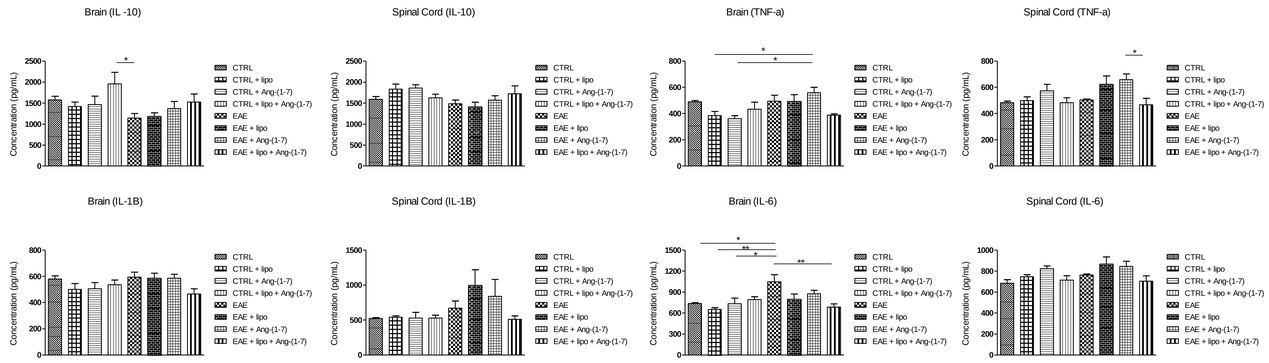
EAE induction
- MOG35-55
- CFA + Mycobacterium tuberculosis H37RA
- Pertussis toxin (2 doses)

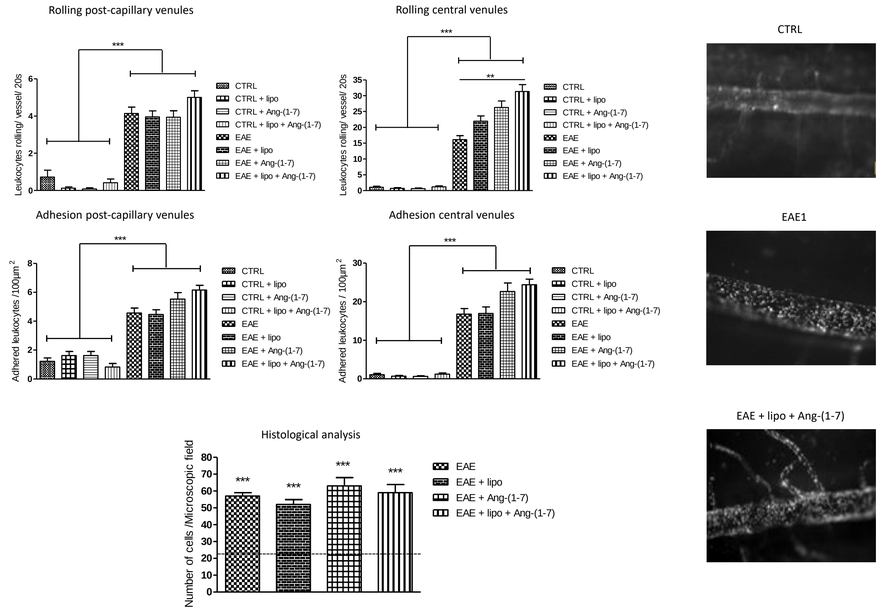
Liposomes had a mean diameter of 133.0 nm and a PDI of 0.3 indicating a monodispersed system.

RESULTS









DISCUSSION

Ang- (1-7) is able to inhibit the NF-kB pathway, causing reduction of inflammatory cytokine levels (BIHL et al., 2015). A study conducted by WU et al. (2015) has shown that administration of icv of Ang- (1-7) in models of middle cerebral artery occlusion (MCAO) reduced the permeability of BBB.

Recent study has demonstrated through the flow cytometry technique that Ang II induces the reduction of Treg cells in the kidneys and blood (CHEN X et al., 2018). Ang-(1-7) in turn, is able to neutralize the proinflammatory action triggered by Ang II (GIRONACCI et al., 2018).

According to ODOARDI (2012), before the entry of autoreactive T cells into the CNS, these establish in the lung, reactivate and acquire the capacity to enter in the CNS.

Conclusion: The nebulization of liposomes containing Ang-(1-7) presents a therapeutic potential, since it was able to attenuate the clinical score and the weight loss in the EAE animals. These Ang-(1-7) treatment effects may be associated with decrease of interleukin 6 (antiinflammatory cytokine) and lowered cerebral and lung vascular permeability.

LITERATURE

Numerous studies have reported the association between cerebral RAS and the development of neurodegenerative diseases (Ang II/AT1 receptor axis).

Liposomes act as a drug targeting system and are able to prevent the rapid degradation of the incorporated substance, promote penetration through the BBB and also exhibit high biocompatibility.

Inhaled delivery of molecules provides direct access to the CNS via the olfactory or trigeminal pathway without necessarily having to transpose the BBB.