# BIO 07 - Enhancement of ANTI-HSV-1 activities using liposomes with naphthoquinones

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## Introduction:

Today almost 67% of individuals with age up to 49 years are infected with HSV-1 and 50% of them, with age between 15-49, are infected with genital HSV-1. Naphthoquinones derivatives synthetized by Mannich base derived possess an efficient ability to control *in vitro* herpesvirus replication. Liposomes are drug delivery systems able to lower the concentrations in order to reduce the toxicity.

## Objective:

Reduce the concentration of 2-aminomethyl-3-hydroxy-1,4-naphthoquinones up to 10 uM coupled to PC-liposomes to be analyzed in pre and post-treatment antiherpetic assays.

## Methodology:

2-aminomethyl-3-hydroxy-1,4-naphthoquinones (0, 5; 1; 5 and 10uM) were incubated in Vero cells for 48 hours to obtain the CC50 values . For all anitival assays HSV-1 was used at MOI of 1 to infect Vero cells at 105 cells/well . Lipid stock solutions of PC (0,1 mM) were prepared in chloroform containing 30% vol methanol. Mixtures of appropriate amounts of PC and aminomethylnaphthoquinones (0,5 to 10 mM) were prepared and chlorophorm was evaporated under a gentle stream of nitrogen. The lipid films were kept in vacuum overnight and hydrated with PBS buffer at pH 7.4 for 1 hour. Then the lipid suspension was freeze-thawed 6 times, LUV were passed 10 cycles through a 100 nm pore size according extrusion method, (LipexTM, Avanti Polar Lipid Inc.). Dynamic light scattering measurements were made to check the size of the vesicles after the extrusion protocol.

**Results:**

The presence of benzyl in the primary amine of naphthoquinone derivatives gives to compound 2 the more toxic structure of the derivatives (11 ± 0,57 mM). Following less toxic are the compound 3 with nitrobenzene substituent and acyclovir, both with the same values of CC50 (13 ± 1,54 and 13 ± 0,88 mM, respectively) and the butyl substituent presented minimum harmful effect (15 ± 0,88 mM). The yield reduction assay showed that nitrobenzene (compound 3) and benzyl (compound 2) substituents conferred 0,36 ± 0,037 mM and 0,56 ± 0,023 mM, more stable than acyclovir (3,16 ± 0,091 mM). Even compound 1 with the lowest antiviral activity of the derivatives (1,73 ± 0,079 mM). The selective index (SI) value of compounds presented higher values than acyclovir (SI = 4,11 mM) with nitrobenzene derivative (compound 3) the most effective antiviral of the series (SI = 36,1 mM), followed by compound 2 (benzene) with SI value of 19,64 mM and compound 1 (n-butil) with 8,67 mM.

**Conclusion:**

The efficacy of compound 3 was evident (85%), followed by compound 1 (70%) and compound 2 (78%). To note is the fact that we have used neutral liposome without any peptide able to maximize the fusion peptide interaction on the membrane of the cell. We concluded with this preliminary study that neutral liposome could carry anti-HSV-1 compounds of naphthoquinone origin.

**Keywords: Nanodrogas; Lipossomos; Antivirais**