has funded a research program that brings together four areas of expertise: the use of plants as natural source for the treatment of disease (ethnopharmacology), the identification and classification of plant species biodiversity, the purification and identification of unique molecules/secondary metabolites of natural origin, and the identification and characterisation of selective inhibitors of virus replication. Three teams, located on Reunion Islands, Mauritius and Madagascar, together with the ICSN, have build a unique sample library consisting out of more than 1500 crude plant extracts that have been evaluated for selective antiviral activity against CHIKV in Leuven and Marseille. Currently, a bio-assay-guided purification of pure substances is in progress, at present yielding the first results. Concomitantly, enzymatic assays are being developed in Marseille to evaluate and possibly characterize in detail the selective inhibitory effect of these compounds.

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63

Synthesis, Influence of Polymer Molecular Weight on Drug Release and Anti-HIV Activity of PEGylated AZT Conjugates

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Despite the first anti-HIV drug zidovudine (AZT) remains an important component in highly active antiretroviral therapy (HAART), the efficacy of its therapy is limited because of short terminal half life (1.2 h) and significant dose-related toxicity, as well as rapid emergence of drug resistance. To overcome its deficiency, one of the strategies was applied in preparation of polymeric AZT prodrug (polymer-AZT conjugate) for improvement AZT pharmacokinetic profiles. In earlier work, we had synthesized a sustained-release prodrug of AZT by conjugating with methoxy poly(ethylene glycol) (mPEG, Mw: 2000 g/mol) and found the conjugate effectively sustained release of AZT, prolonged half life and decreased toxicity in vitro. In order to elucidate the influence of molecular weight of mPEG on biological and pharmacokinetic properties, we synthesized a series of mPEG-succinyl-AZT conjugates with different molecular weight of mPEG (Mw: 750, 2000, 5000, or 10,000 g/mol). Drug release assay indicated that the mPEG-succinyl-AZT conjugates were capable of releasing the parent drug in sustained profiles, but there was no clear molecular weight-correlation to be found. The newly synthesized conjugates were also evaluated for anti-HIV activities and cytotoxicity in MT-4 cells. All of the conjugates displayed good activity against HIV replication. Especially for $mPEG_{750}$-succinyl-AZT (2a), it exhibited good inhibition to both wild and mutant strains including K103N and RES056, which were in the same order as the activity of AZT, but its cytotoxicity was lower than AZT. The selectivity index (SI) showed a clear correlation to Mw of mPEG, i.e. the higher Mw of mPEG-succinyl-AZT, the lower SI of the conjugate. In all, $mPEG_{750}$-succinyl-AZT (2a) exhibits better drugability than other polymeric conjugates, which might provide a feasible sustained-released prodrug alternative of AZT in antiretroviral therapy.

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64

The Protective Action Arbivirin and Aminocaproic Acid during the Experimental Influenza

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The anti-influenza preparation Arbidol is produced in Ukraine under the name of Arbivirin (Ar). It is officially approved and recommended for the prophylactics and treatment of influenza and acute respiratory viral infections (ARVI) in adults and children aged 2 years and more and aminocaproic acid (ACA) is recommended in adults and children without age limits.

Objectives: Study of the anti-influenza activity preparations on the model of the acute influenza infection in mice.

Methods: We have used: high virulent strain of influenza virus A/PR/8/34 (H1N1), adapted to the mice lungs, 11-days chicken embryos, inbred white mice of 15–18 g weight, ACA and Arbidol (substance Zdorovya pharmaceutical company). The animals from experimental and reference groups were infected intranasally under light aether narcosis with 0.05 ml viral solutions in concentrations from 1×10^{-2} to 1×10^{-7} (4 mice for each solution). The animals from reference group have obtained the day before infection, the infection day and the 3 following days the 0.2 ml of placebo (1% starch solution) twice a day *per os*. The mice of the experimental group have obtained the Ar taken in ratio of 60 mg/kg per day added to the 1% starch solution according to the same scheme as the placebo in the reference group was introduced. The mice of the experimental group obtained ACA in ratio of 2 g/kg per day. The death of animals in each group was accounted during the 14 days after infection.

Results: The results obtained certify that LD_{50} in the reference group was equal to 5.75 lg. In the ACA provided group, the LD_{50} was lower by 1.5 lg, and in group Ar by 1.25 lg lower than in the reference group. The mortality was in the ACA group lower by 27%, and in Ar group by 21% lower than in the reference group. The average longevity was in the ACA group was higher by 1.4 days (9.9 days) and in Ar group by 1.9 days higher (10.4 days) than in the reference group (8.5 days).

Conclusions: The use of ACA and Ar according to the prophylactics/treatment scheme has caused the pronounced protective effect during the modeling of the influenza infection in mice.

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65

Oseltamivir Influences Hepatic Cytochrome P-450 Dependent Oxidative Metabolism in Influenza Virus Infected Mice

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Osletamivir is known as a neuraminidase inhibitor with a highly specific action against influenza A and B viral infections. Designed as a structural analogue of neuraminic acid, oseltamivir competitively binds the active site of the enzyme neuraminidase on the influenza virus surface. Then, it realized its antiviral effect. The purpose of this study was to examine the impact of oseltamivir