showed a high improvement in aqueous solubility together with an efficient conversion to the biologically active parent drug in the presence of DPPIV/CD26 and in serum.

We now explore the viability of this DPP-IV/CD26 prodrug approach in a variety of hydroxy-containing drugs of different nature (primary, secondary, tertiary or aromatic hydroxyl groups). A broad variety of prodrugs have been designed synthesized and evaluated for their pharmacokinetic properties including chemical and enzymatic stability (cleavage rates) and water solubility. The results indicated that the prodrugs are efficiently converted to the parent drugs, several of them showed markedly increased water solubility. Thus, the results support the wide applicability of our prodrug approach.

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Synthesis and evaluation of biological activity of new aminoadamantane amides containing hydroxycinnamoyl moiety

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In humans, oxidative stress is involved in the pathogenesis of many diseases, including such as influenza virus infections. Therefore antioxidants are those molecules potentially applicable in prevention from flu. The hydroxycinnamic acids and their derivatives are natural antioxidants with multiple mechanisms of action. The compounds are known to have a variety of activities: antiviral, antibacterial, immunostimulatory and etc. In order to obtain new potent antiviral drugs, we connect two pharmacophores with proved antiviral activity such as antiviral drugs – aminoadamantane derivatives and hydroxycinnamic acids. Amidation of hydroxycinnamic acid with amantadine or rimantadine was carried out using EDC/HOBt as peptide coupling method. The structures of the obtained amides were characterized by spectral methods (UV, ^{1}H NMR, MS). The evaluation of antiviral and antiradical activities of synthesized amides is in progress.

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Coumarins Hybridized with Heterocycles or Ribonucleosides for Eradication of Hepatitis C Virus

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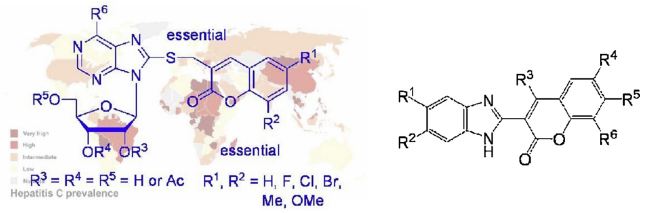
Coumarin moiety conjugated with a benzimidazole moiety by a –SCH_2– linker would exhibit potent inhibitory effects on HCV. Consequently two series of analogues were synthesized to constitute new compound libraries by incorporation of heteroatoms into the benzimidazole moiety. Some of these coumarin–heterobicycle conjugates possessed appealing antiviral activities with significant selectivity index values. Lack of the sulfur atom-containing linkage led to poor biological activities. Prominent examples included coumarin conjugates containing an imidazopyridine, purine, or benzoxazole moiety they were found to inhibit HCV replication at an EC_{50} value of 6.8, 2.0, and 12 mM, respectively. Furthermore, the conjugation was extended to compounds with three components: coumarin, purine, and ribofuranose. The essential functional groups and moieties therein will be discussed.

Our laboratory has successfully established three compound libraries. Through analysis of the data therein, we came up with their structure–activity relationships (SAR). In this talk, we report our design and synthetic strategies on obtaining the targets and their SAR. These new findings provide a hybridization approach of value for drug development in the future.



Further reading

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HSV-1 and Alzheimer's Disease: The Case for Antiviral Treatment

Withdrawn

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Synthesis and Antiviral Evaluation of N^9-[2-(Phosphonomethoxy)ethyl] (PME) Analogues Derived from 8-Substituted Purines

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Structure–activity relationship (SAR) studies have shown that the nature of the heterocyclic base plays a determining role in the biological activity of the acyclic nucleoside phosphonates (ANPs). This activity is connected especially with purine derivatives, the only exception being the cytosine derivative HPMPC. It was also shown that mostly compounds derived from purines containing a free amino group were active (adenine, guanine, 2-aminopurine