mulation of a relatively high concentration (1 mg/g) in vaginal gels, the present study suggests precipitation of the active ingredient in the vaginal environment. Thus, solubilizing excipients are required to avoid precipitation and to preserve the antiviral activity of saquinavir. This study illustrates the importance of evaluating the pharmaceutical availability of poorly water-soluble microbicide candidates in biorelevant media.

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Identification of Antiviral Activity of Koe Ken Tang Against Influenza Virus

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Influenza still remains the major plagues as well as the highly pandemic outbreak in the world. Due to the emergence of neuraminidase (NA) and M2 inhibitor resistant viruses in current clinical reports, we have sought to find out the traditional prescriptions used in thousands of years in China to manage the pandemic of influenza viruses. In this study, we have demonstrated that the Chinese herbal mixture Koe Ken Tang (KKT) could not only inhibit cytopathy of MDCK cells but also block the synthesis of cleavage PARP induced by influenza A virus. In addition, according to time of addition assay, we notice that KKT exerts anti-viral effects after viral infection, but does not lead to a general block of transcription/translation or inhibition of viral polymerase activity based on the vRNP activity inhibition assay and primer extension assay. We also figure out that KKT could exert antiviral activity in multiple flu A strains, including Tamiflu resistant virus, but not flu B. Finally we have demonstrated that KKT could suppress the Akt phosphorylation post viral infection and decrease the titers of progeny virus. By IF, we observe that KKT could block the NP export from the nucleus at 9 h post-viral infection. These data suggest that the antiviral effects of KKT was due to its suppression of Akt phosphorylation that leads to viral NP protein accumulation in the nucleus and thus offer the potential for development of a new anti-influenza virus agent.

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Anti-influenza Virus Activity by Tricin, Isolated from Sasa Albomarginata in Japan

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Effective new anti-influenza virus agents need to be developed. We examined the in vitro anti-influenza virus properties of tricin, 4′,5,7-trihydroxy-3′,5′-dimethoxyflavone, isolated from Sasa albomarginata, a bamboo known in Japan. The effects were studied on influenza virus A/Solomon islands/3 (H1N1) and B/Malaysia/2506 replication in the Madin-Darby canine kidney (MDCK) cells. In a plaque-reduction assay, tricin showed dose-dependent inhibitory effects at concentrations ranging from 0.37 μM to 10 μM. The predominant inhibitory effect of tricin treatment was observed during 1–3 h after viral infection using time of drug addition assay. Moreover, tricin inhibited the synthesis of viral RNA but had no virucidal effect on cell-free virus (HINI). Western blot analysis demonstrated that tricin decreased the amount of HA and M proteins expression in the infected cells. These findings indicate that tricin acts on a late stage of the viral replication cycle resulting in inhibition of progeny virus production from the infected cells. It suggests that tricin is a novel compound with potential anti-influenza virus activity. Future studies should evaluate these findings in vivo.

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Synthesis and Biological Evaluation of Triazolo-pyrimidine Derivatives as Novel Inhibitors of Hepatitis B Virus Surface Antigen (HBsAg) Secretion

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Due to the side effects of interferon and the viral resistance to nucleos(t)ide inhibitors of the viral polymerase, current therapies for chronic hepatitis B virus (HBV) infection are still far from satisfactory. Further development of more effective therapeutics needs antiviral drugs that could interfere the viral life cycle through blocking other functions than inhibiting the viral polymerase, whether for monotherapy or combination therapy. The high levels of hepatitis B virus surface antigen (HBsAg)-bearing subviral particles in the serum of chronically infected individuals are thought to play an important role in suppressing the HBV-specific immune response. Inhibitors of HBsAg secretion could enable the therapeutic use of HBV vaccines or be used as combination therapy with nucleoside drugs for the treatment of HBV infection. However, current therapeutics are not directed at reducing this viral antigenemia. In order to achieve this therapeutic goal, our recent high-throughput screening of an in-house small-molecule library identified HBF-0259, 7-(2-chloro-6-fluorophenyl)-5-(4-chlorophenyl)-4,5,6,7-tetrahydro-tetrazolo[1,5-a]pyrimidine, as an effective inhibitor of HBsAg secretion, using the HBV-expressing cell line HepG2.2.15. During our follow-up lead optimization, a series of novel triazolo-pyrimidine anologues of HBF-0259 were synthesized and evaluated for their in vitro inhibitory activity of HBsAg secretion. No cytotoxicity was observed for these compounds at the concentration up to 50 μM. PBHBV-2-15 was identified as the most potent inhibitor ($EC_{50} = 1.40 \pm 0.41$ μM). PBHBV-001, PBHBV-2-1 and PBHBV-2-15 also exhibited good activities against nucleoside resistant mutants. Now, two analogues, PBHBV-001 and PBHBV-2-15 are undergoing in vivo toxicity and efficacy study.

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