amino acid insertion within CHKV nsP2. The replicon cell line was characterized and adopted for antiviral screening in 96-well plate format. The hit compounds identified against SFV were assayed in the replicon system, and the flavonoids apigenin, chrysin, naringenin and silybin were found to suppress CHKV replicon expression levels. The stable replicon cell line developed in the course of this work is a highly useful tool in studies of CHKV replication inhibitors. Recently, we have validated the CHKV replicon cell line for screening in a fully automated 384-well format, and initiated screening of larger chemical libraries.

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New Antiviral Substances of Indoloquinoxaline and Diphenyl Nature

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A range of newly synthesized indoloquinoxaline and diphenyl derivatives was tested for toxicological, antiviral (AV) and interferon-inducing properties in attempt to develop novel AV substances with lower toxicity, higher effectiveness and different pattern of biological properties than that of current medications. Tilorone dihydrochloride was chosen as reference substance. 6-[3-(4-Morpholine)ethyl]-6H-indolo[2,3-b]quinoxaline dihydrochloride and 4,4′-bis-[2-(diethylamino)ethoxy]diphenyl dihydrochloride, further referred to as I1 and D1, demonstrated the best properties. In vitro experiments were carried out on L929, EPT cell cultures, splenic and peritoneal ex vivo murine cells. Test substances turned to be significantly less toxic than official preparation. Maximum tolerable dose for D1 and I1, determined on L929 cells, was 5× and >37× higher than that of tilorone. This tendency repeated in acute toxicity tests on mice; both substances can be classified as low toxic. IFN-inducing activity in case of all tested cell cultures and 3 preparations was most efficient at 6 mkg/ml. Achieved IFN titers were also similar, which indicates certain common mechanisms of action. In vivo D1 stimulated much higher IFN titers in serum than tilorone, while I1 possessed similar effectiveness. Both test substances activated cellular link of immunity more intensively and differed from each other and reference drug by the cytokine profile. AV effect was observed in vitro and in vivo for both test agents. It was not exclusively mediated through IFN system, but was at least partly based upon direct AV properties against RNA and DNA containing viruses. I1 was more efficient in prophylactic application, while D1 and tilorone were active in case of therapy as well. Expressed antiviral properties, pronounced IFN-stimulating and immunomodulating potential allow us to consider both tested substances as novel antiviral drugs. Low toxicity and wide range of effective concentrations grant certain advantages over official AV drug–tilorone.

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Pegasys As A Second Line of Effective Treatment Plan for G3 Non Responders of Conventional Therapy

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In Pakistan most common Genotype is 3a and above 70 percent response to 24 weeks treatment plan has been observed in our previous study (Raza et al., 2010). Available treatment plans (TPs) in Pakistan are: combinational treatment of conventional interferon 3MIU plus Ribavirin 1200 mg/day for 24–48 weeks (TP-1), Pegasys 180 μg/week plus Ribavirin 1200 mg/day for 24 weeks as a first line of treatment (TP-2), Pegintron 180 μg/week plus Ribavirin 1200 mg/day for 24 weeks as a 1st line of treatment (TP-3), Pegasys 180 μg/week plus Ribavirin 1200 mg/day for 24 weeks as a 2nd line of treatment (TP-4) for non responders of TP-1. Four available treatment plans (TPs) are compared to have the comparative effectiveness against HCV genotype 3a. In this cohort study, patients were categorized into four groups as stated above. Included study subjects were 25, 25, 20 and 22 for groups 1–4 and were given treatment plans 1–4, respectively. Viral load before and after the treatment were performed on Rotorgene 3000™ Real Time PCR system using AJ Roboscreen extraction and quantification modules. Response rate was found 76, 80 and 80 and 81.8% in four treatment plans. Study data suggests that for non responders of conventional therapy, pegasys therapy will be effective as a 2nd line of treatment plan. This will also help in counciling the HCV on treatment patients to adhere to therapy.

Reference

Raza, A., et al., 2010. Therapeutic response guided Interferon (IFN) therapy among patients chronically infected with hepatitis C virus. Antiviral Research 86, A1–A78.

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Effective Treatment Plan for G3 Patients

Withdrawn

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Cost Effective Rapid Virological Response Guided Peginterferon Therapy Plan in HCV Genotype 3 Pakistani Population

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Being poor country standard care of treatment in Pakistan against Hepatitis C is conventional interferon combination therapy. But response rate against genotype 3 has been found ~65% in our previous studies. Peginterferon therapy is highly expensive. It is important to tailor the treatment plans on individual