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Antiviral-Immunomodulator R-837 Induces 2,5-Oligoadenylate Synthetase (2,5 AS) Activity In Mononuclear Cells Of Treated Guinea Pigs. C.E. Weeks, S.J. Kruger and S.J. Gibson. 3M/Riker Laboratories, Inc., St. Paul, MN 55144-1000 USA.

R-837 (1-isobutyl-1H-imidazo[4,5-c]quinolin-4-amine) is an effective antiviral agent in a Herpes simplex virus (HSV) infected guinea pig (gp) model. Interferon (IFN) is detected in serum of R-837 treated gp (26th ICAAC, abst No. 385). IFN regulates 2,5 AS which can produce antiviral effects. Following oral dosage to 200-250 g female Hartley gp, 2,5 AS activity is determined in isolated blood mononuclear cells. The assay uses poly I:C agarose beads, [^{3}H] - ATP, bacterial alkaline phosphatase, and DEAE cellulose filtration. 2,5 AS activity induction is dose related. At 48 hr post dose, levels [units (U)=nmoles/mg protein/h] are 0.55 at 1.0 mg/kg; 3.56 U, 3.0 mg/kg; and 2.32 U, 5.0 mg/kg. Time course studies demonstrate activity peaks about 96 h after a 5 mg/kg dose (4.21 U) and is elevated vs control through 144 h (3.51 U). Control 2,5 AS levels vary; average, 0.62 U. HPLC analyses of assay extracts were used to identify and verify production of 2,5 A core polymers. An analog with no anti-HSV activity does not induce 2,5 AS activity. S-26704, the active metabolite, provides 5.98 U vs control (1.18 U) at 24 h following a 5 mg/kg oral dose. Poly I:C at 3 mg/kg IV is a weaker 2,5 AS inducer: 0.80 U vs 0.26 U (control) at 48 h. In vitro 0.1 mM R-837 does not inhibit thymidine kinase, DNA polymerase, or S-adenosylhomocysteine hydrolase activities. Thus we conclude that 2,5 AS induction is a principal part of the antiviral mode of action of R-837.

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Antiviral Acivities of Immuno-modulating Agent ACPS in cell cultures and in mice.Hongshan Chen[1], Zhuang Li[1], Li Teng[1],Pei-fen Lin[2], Ju-ming Zhang[2],Institute of Medicnal Biotechnology Chinese Academy of Medical Sciences,[1] Institute of Molecular Medicne, Zhe-jiang College of Chinese Traditional Medicne[2],People's Republic of China

ACPS, polyssacharide complex extracted from roots of Actinidia chinensis Planch, was proved to be an immunomodulating agent. It activated NK cells,macrophages, enhanced specific antibodies and induced interferon in mice. ACPS inhibited influenza and herpes viruse replication in cell cultures, IC_{50} for influenza virus H_0N_0 WS strain, H_3N_2 YF 72-243and B T-8413 in MDCK cell cultures were 318, 620 and 595 μg/ml respectively, HSV were less susceptible to ACPS than influenza viruses, 1000 μg/ml ACPS inhibited 46.24% and 31.39% of HSV-1 and HSV-2 in vero cell cultures respectively. ACPS protected mice from intravenous infection of influenza virus H_3N_2 and also HSV-1 Sm-44, decreased mortality and prolonged the life span when given to mice intraperitoneally 24 hrs before infection, ED_{50} for influenza virus was 9.65± 2.67 mg/kg and for HSV-1 was 18.15 ± 5.37 mg/kg. It also prolonged the survival time of mice bearing Erhlich ascitic carcinoma or mouse leukemia P-388, it also decreased the growth of solid liver cancer in mice. ACPS decreased the mortality of E. coli and Staphylococcus aureus infection in mice. ACPS showed broad spectra of biological activities: antiviral, anti-cancer and anti-bacterial in vivo, all of these might be due to its immuno-modulating mechanism.