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Reduction of Respiratory Syncytial Virus (RSV) Shedding in African Green Monkeys Treated with SP303. K.F. Soike, J.-Y. Zhang and L.R. Meyerson, Tulane Regional Primate Research Center, Covington, LA USA and Shaman Pharmaceutical Inc., San Carlos, CA USA.

Respiratory syncytial virus (RSV) infects African green monkeys following combined intratracheal and intranasal inoculations to produce infection of both the upper and lower respiratory tract. Infection is evaluated by quantitating RSV in daily oropharyngeal swabs and by noting clinical symptoms. This animal model has been used to determine antiviral activity of SP303, a natural product which is a polyphenolic polymer, MW=2000 daltons. Intravenous (i.v.) administration of SP303 was begun 4 hours before virus inoculation and continued twice daily for seven days at doses of 1.0, 0.5 or 0.2 mg/kg/day. Titrations of throat swabs showed a dose related reduction in RSV titers compared to untreated controls on each of nine days of virus shedding. SP303 treatment at 1.0 mg/kg/day i.v. begun 4 hours before virus inoculation or at 24 or 48 hours after virus inoculation showed antiviral efficacy only when treatment preceded virus inoculation. Oral treatment by gavage reduced daily throat swab titers of RSV at doses of 270, 90 and 30 mg/kg/day when begun 4 hours before virus inoculation and given twice daily for 7 days. Reduction in titers correlated with dose. Toxicity evaluated by daily clinical examination and hematologic tests was not seen when groups of three monkeys each received either oral, i.v. bolus, or i.v. one hour infusions of SP303 at 5 mg/kg/day for 5 consecutive days. No toxicity was observed in groups of two monkeys treated by gavage for five days with doses of 100, 300, or 900 mg/kg/day. Clinical chemistry tests performed on these monkeys were unremarkable. SP303 has been shown to be effective in reducing titers of RSV in the upper respiratory tract of experimentally infected monkeys. SP303 was not toxic at doses exceeding the maximum efficacious dose employed.

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Combined Antiviral and Antimediator Treatment for Common Colds. J.M. Gwaltney, Jr., M.D., Department of Internal Medicine, University of Virginia Health Sciences Center, Charlottesville, VA, U.S.A.

Background. Combinations of an antiviral agent and multiple anti-inflammatory compounds were used in two blinded, placebo controlled studies to treat experimental rhinovirus colds.

Methods. In the first study, intranasal interferon α-2 (3 million units) and ipratropium (80μg) and oral naproxen (500 mg loading dose and then 250 mg) were begun 24 hr after rhinovirus inoculation and continued three times a day for four days. Volunteers were monitored by viral culture, serum neutralizing antibody response, symptom scoring, and nasal secretion weights. In the second study, topical phenylephrine Hcl ¼% and chlorpheniramine maleate 4 mg were added to the combination.

Results. In the first study, mean (± SEM) viral shedding was 4.4 ± 0.3 days for control and 2.8 ± 0.3 days for treated volunteers ($p = <0.003$). Geometric mean virus titers were lower on days two and three in treated than control subjects ($p \leq 0.03$). Serum antibody responses and post-infection geometric mean antibody titers were similar in both groups ($p=>0.1$). Colds developed in seven of 17 (41%) and seven of eight (88%) of treated and control subjects, respectively ($p = 0.04$). Mean total symptom scores (± SEM) were 9.4 ± 2.2 and 24.9 ± 2.8 in treated and control subjects, respectively ($p = <0.001$). Rhinorrhea ($p = 0.08$), nasal obstruction ($p = 0.015$), sore throat ($p = <0.001$), cough ($p = 0.05$), headache ($p = 0.01$), and malaise ($p = <0.001$) were less severe in treated subjects. Mean (± SEM) nasal secretion weights were 12.9 (± 4.8) gm in treated and 20.3 (± 5.4) gm in control subjects ($p = 0.4$). In the second study, mean (± SEM) rhinorrhea scores were 0.9 (± 0.6) and 3.8 (± 1.6) ($p = 0.08$) and mean (± SEM) nasal secretion weights were 1.6 (± 0.6) gms and 22.2 (± 12.9) gm ($p = 0.08$) in treated and placebo groups, respectively. Medications were well tolerated.

Conclusion. Combined antiviral and antimediator treatments were more effective than previously reported treatments for experimental colds.