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FILE: ▪Ivy (*Hedera helix*)
▪Pediatric Asthma
▪Bronchial Asthma

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RE: Ivy Extracts (*Hedera helix*) in Pediatric Bronchial Asthma

Hofmann D, Hecker M, Völp A. Efficacy of dry extract of ivy leaves in children with bronchial asthma—a review of randomized controlled trials. *Phytomedicine* 2003;10:213-220.

Bronchial asthma is the most prevalent form of chronic airflow obstruction (CAO) in children and adolescents, the symptoms of which can lead to "serious restrictions in daily activities." Herbal expectorants, most of which are based on extracts from ivy (*Hedera helix*) or thyme, are popular in Europe because of their "good risk benefit ratio" and "comparatively moderate" cost. Despite their popularity, the clinical efficacy of ivy extracts is disputed because evidence for their mucolytic and secretolytic effects is lacking. However, preclinical studies by Bedir et al. (2000), Cioaca et al. (1978), Hen et al. (1996), and Trute et al. (1997) suggest that ivy leaf extracts have spasmolytic, bronchodilating, and antibacterial effects, which are mainly due to their content of triterpene saponins.

The authors' objective was to provide a comprehensive review of clinical evidence of the mucolytic and secretolytic activity of ivy leaf extracts in children with bronchial asthma. This review was based on published data as well as original data from clinical trials. Trials were considered eligible if the participants were children with CAO who had provided written informed consent, if the intervention included the use of ivy leaf extracts, and if the trial were randomized and included a placebo or a reference control group. MEDLINE (1966–2001) and EMBASE (1974–2001) searches were conducted to identify eligible trials using the search terms "ivy," "*Hedera helix*," and "Efeu." ("Efeu" is German for "ivy.")

Three randomized controlled trials met the eligibility criteria: two by Mansfield et al. (1997 and 1998) and one by Gulyas et al. (1997). All three trials had used the same product (Prospan®; 30% ethanol and a drug-extract ratio of 5:7.5:1), which was manufactured by Engelhard Arzneimittel GmbH & Co., Niederdorfelden, Germany. In addition, the participants in all three of the trials had bronchial asthma, and airway resistance (R_{AW}) was the main outcome measure.

Mansfield et al. (1997)
Twenty-six boys and girls aged 4-12 years participated in this open crossover study. The children consumed Prospan-containing cough drops (35 mg ivy leaf dry extract/day) or cough suppositories (160 mg ivy leaf dry extract/day) for 3 days. The mean (± SD) area under the curve (AUC) for R_{AW} on day 3 was 1.86 ± 0.67 kPa/L/sec with the cough drops and 1.79 ± 0.79 kPa/L/sec with the suppositories.

Mansfield et al. (1998)
Twenty-four boys and girls aged 4-12 years participated in this double-blind crossover study. The children consumed Prospan-containing cough drops (35 mg ivy leaf dry extract/day) or placebo for 3 days. The mean (± SD) AUC for R_{AW} decreased from 0.74 ± 0.24 kPa/L/sec before treatment with the cough drops to 0.61 ± 0.25 kPa/L/sec on day 3 and from 0.69 ± 0.24 to 0.67 ± 0.23 kPa/L/sec after the placebo. The treatment difference was significant (P = 0.04; two-sided exact Wilcoxon test).

Gulyas et al. (1997)
Twenty-five boys and girls aged 10-16 years participated in this double-blind, double-dummy, crossover study. The children consumed Prospan-containing cough drops (42 mg ivy leaf dry extract/day) or syrup (105 mg ivy leaf dry extract/day) for 10 days. The mean (± SD) AUC for R_{AW} decreased from 3.74 ± 0.86 kPa/L/sec before treatment with the cough drops to 3.39 ± 1.04 kPa/L/sec on day 10 and from 3.77 ± 0.95 to 3.39 ± 1.02 kPa/L/sec after the syrup. The treatment difference was not significant.

Interstudy comparison
All ivy treatments resulted in significant improvements in all parameters investigated. The Prospan-containing cough drops were the most efficacious of the treatments studied. The ivy leaf-containing suppositories and syrup were "significantly superior" to placebo, and no significant changes from baseline were observed in the placebo group. Only in the 1997 study by Mansfield et al. was there a possible adverse reaction (i.e., exacerbation of atopic dermatitis) to the ivy leaf treatment.

Conclusion
The authors concluded that the trials reviewed "indicated that ivy leaf extract preparations show effects respective to improving the respiratory function of children with chronic asthma." However, only one of the reviewed trials was placebo-controlled and, therefore, more "far-reaching conclusions are limited." Further research—particularly long-term, placebo-controlled trials—are needed.

—Brenda Milot, ELS

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