PROSPAN®

For chesty coughs to decrease mucus, clear congestion, soothe airways & relieve inflammation

The Prospan® range difference

- The Prospan® range features a clinically trialled extract of *Hedera helix* - EA 575.
- Prospan® has been used for more than 20 years worldwide to help clear mucus from the airways and relieve chesty coughs.
- Prospan® is backed by rigorous clinical evidence in over 65,000 patients, demonstrating excellent efficacy and tolerability.
- With 65 years of research and innovation, the Prospan® range is produced using a patented process that helps ensure every batch has the same reliable EA 575 formula.
- Conforms to well-established use by the European Medicines Agency (EMA) as an expectorant in case of productive cough.
- The Prospan® range contains non-drowsy, sugar-free formulations, suitable for all ages (medical advice is recommended for children aged 2 years and younger).
- Prospan® is very well tolerated and pleasant tasting.

The Prospan® range contains the scientifically researched extract of *Hedera helix* - EA 575

The Prospan® range therapeutic indications

IN ADULTS AND CHILDREN:

- Decreases excess mucus.
- Loosens chest phlegm and helps clear respiratory tract mucus.
- Reduces mild upper respiratory tract congestion.
- Increases cough productivity.
- Relieves coughs.
- Relieves mild bronchial mucus congestion, irritation and cough.
- Soothes the respiratory tract mucus membranes.
- Is anti-inflammatory.

EA 575 – the ivy leaf extract clinically researched to relieve the symptoms of chesty coughs

Multiple clinical trials and history of use show efficacy and tolerability

Prospan® has a long history of use and high levels of tolerability:

- Prospan® is backed by years of research in more than 65,000 patients to help clear mucus from the airways and relieve chesty coughs
- Prospan® is well tolerated as demonstrated in numerous clinical trials

The Prospan® range research summary

Prospan®, and the specialised extract EA 575, have been studied for efficacy and tolerability in thousands of patients over many years.

Lead Author/Year	Study Design	Subjects / Dose	Outcome Summary
Schaefer A, et al. 2019[1].	Randomised, placebo-controlled, double-blind, multicentre, study.	209 adults with acute bronchitis (aged 18-73 years; mean 36 years).Prospan® taken either two (7.5mL) or three (5mL) times daily, or placebo, for 1 week, with a total observational period of 2 weeks.	**Efficacy and tolerability study** This study showed the efficacy and tolerability of either dose regimes (total 15mL per day), with a favourable impact on the outcome of subjects in acute bronchitis. Both dosage schemes (5mL three times daily or 7.5mL twice daily) were found equally efficacious. Additionally, there were sustained benefits for cough severity, even after Prospan® treatment cessation. Prospan® was well tolerated.
Fazio S, et al. 2009[2].	Prospective, open, multicentre post-marketing study.	9657 adults and children with acute or chronic bronchitis. (5181 children, median 5.5 years; and 4476 adults, median 41.9 years). Prospan® for 7 days, with the following regime: a. 0-5yrs: 2.5mL 3 times daily b. 6-12yrs: 5mL 3 times daily c. >12 and adults: 5-7.5mL 3 times daily.	**Large efficacy and tolerability study** After 7 days of therapy, the majority of patients (95.1%) experienced significant symptom improvements. Cough and expectoration improved or resolved in 93% of patients and shortness of breath and chest pains improved or resolved in 91% of patients. Prospan® was well tolerated in all age groups.
Schaefer A, et al. 2016[3].	Randomised, placebo-controlled, double-blind, multicentre study.	181 adult patients with productive cough (aged 18-75 years). Prospan® 5mL, or placebo, 3 times daily for 7 days.	**Efficacy and tolerability study** This clinical trial showed Prospan® to have statistically significant and clinically relevant effects in the treatment of acute cough. Benefits were seen within 48 hours of treatment, with a significant treatment advantage over placebo remaining 7 days after stopping Prospan®. Prospan® was well tolerated.
Lang C, et al. 2015[4].	Non-interventional study	1,066 children with acute bronchitis (aged 6-12 years). Prospan® in five different forms, for 7 days: a. Syrup (n=719) b. Drops (n=64) c. Liquid (n=196) d. Effervescent tablets (n=38) e. Cough lozenges (n=49). Dosage was acording to package leaflet.	**Large efficacy and tolerability study** The Bronchitis Severity Score (BSS) improved considerably by 79.3%, with no relevant differences between the different forms. Particular improvements were noted in symptoms such as shortness of breath and coughing up of mucus. Clear reduction in chest pain upon coughing and a drop in the number of nocturnal sleep issues were also reported. Improvement in symptoms was demonstrated after as little as 3.48 days. Prospan® was well tolerated.

EA 575 conforms to EMA standards

The well-regarded European Medicines Agency (EMA) Committee on Herbal Medicinal Products (HPMC) reported in 2017 that the EA 575 extract conforms to the requirements for the well-established use as an expectorant in cases of productive cough.[5]

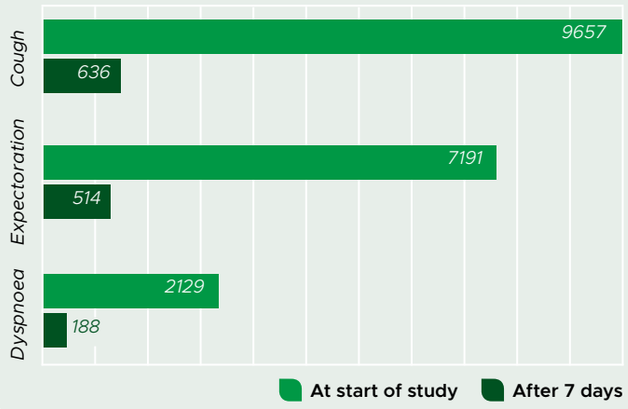
Prospan® relieves chesty cough symptoms in children and adults

In this large study (n=9657) of children and adults, Prospan® treatment improved or resolved overall symptoms (cough, expectoration, dyspnoea and chest pain) in 95.1% of subjects.

Cough and expectoration improved or disappeared in 93% of patients and dyspnoea and chest pains improved or disappeared in 91% of patients.[2]

Fazio S et al. Tolerance, safety and efficacy of *Hedera helix* extract in inflammatory bronchial diseases under clinical practice conditions: a prospective, open, multicentre postmarketing study in 9657 patients. Phytomedicine 2009;16:17-24.

Number of patients with symptoms before and after Prospan® treatment[2]

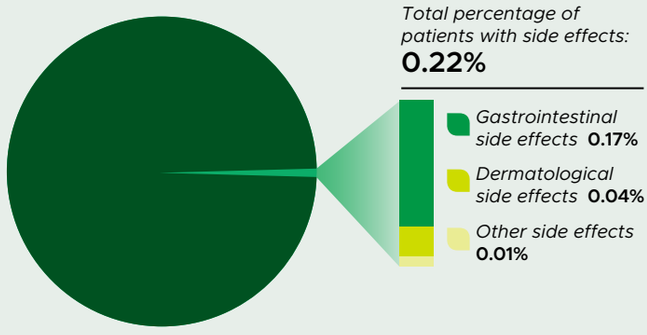


High levels of tolerability with Prospan® in 52,478 children with respiratory illness

This retrospective survey confirmed the outstanding tolerability of Prospan® in a very large group of children aged 0-12 years. The incidence of side effects was an incredibly low 0.22%, which were mainly gastrointestinal symptoms (0.17%).[6]

Kraft K. Tolerability of dried ivy leaf extract in children. Zeitschrift für Phytotherapie 2004; 25:179-81.

Tolerability of Prospan® cough syrup in children[6]



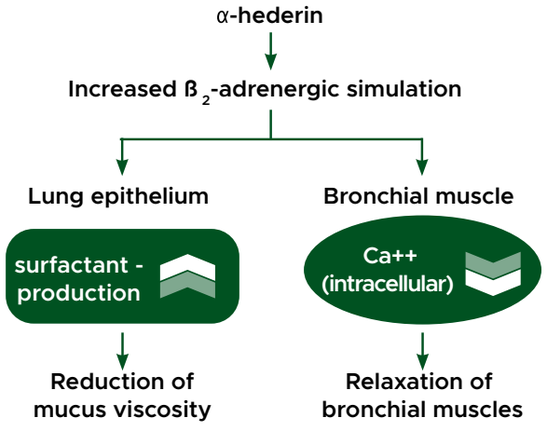
The Prospan® range potential modes of action

The proposed mode of action for Prospan® in the respiratory tract is linked to ß2 adrenergic receptors. Scientific studies suggest that saponins from Helix hedera, such as α-hederin, inhibit the inactivation of ß2 receptors in the lungs and bronchi. This inhibition is attributed to the secretolytic and bronchospamolytic effects of Helix hedera.

Increased ß2-adrenergic receptor activation creates an intensified adrenaline signal, which causes the epithelial cells of the lungs to form more surfactant; thereby, reducing surface tension and lowering mucus viscosity. This makes the mucus easier to cough up. This secretolytic action then exerts a soothing and cough-relieving effect on the bronchi.[7]

These receptors are also found on the cells of non-striated bronchial muscles. The increased adrenaline receptivity, by Helix hedera, increases cAMP concentration resulting in a drop in intracellular concentration of calcium. This leads to relaxation of the cramped bronchial muscles.[7,8]

Recent research has also elucidated to a mechanism underlying the anti-inflammatory effects of EA 575®, which is based on the reduced migration of NFκB into the cell nucleus. This anti-inflammatory effect may play a role in human lung epithelium cells and; therefore, in acute and chronic inflammation of the airways.[9]



Active ingredients

Prospan®, Prospan® Menthol and Prospan® for Children: (per 5 ml) *Hedera helix* extract dry conc. 35 mg equiv. to dry leaf 218.75 mg (EA 575).

Prospan® Drops contains (per 24 drops) *Hedera helix* extract dry conc. 24 mg equiv. to dry leaf 150 mg (EA 575).

Prospan® soft lozenges contain (per lozenge) *Hedera helix* extract dry conc. 26 mg equiv. to dry leaf 163 mg (EA 575).

Dosage and administration

Prospan® & Prospan® for Children:
Adults: 5-7.5mL three times a day. 2-5 yrs: 2.5mL three times a day, 6-16 yrs: 5mL three times a day.

Prospan® Menthol:
Adults & children over 11 yrs: 5mL three times a day. 6-11 yrs: 5mL twice a day.

Prospan® Lozenges:
Adults & children over 12 yrs: 1 lozenge four times a day. 6-11 yrs: 1 lozenge two times a day.

Prospan® Drops:
Adults & children over 12 yrs: 24 drops three times a day.

Benefits can be expected after 7 days.

Storage conditions

Keep the Prospan® range cool dry place where the temperature stays below 30°C.

Check the date of recommended use on the product packaging and consumer information sheet.

Prospan® Drops: dark suspended particles may form in the liquid and the taste of the preparation may also vary slightly; however, the quality of the product is not affected.

Contraindications and precautions

Do not recommend if there is a history of hypersensitivity to *Hedera helix*.

Prospan® contains sorbitol and potassium sorbate. Products containing sorbitol may have a laxative effect or cause diarrhoea.

Prospan® Drops contains 47% alcohol. No other product in the Prospan® range contains alcohol.

There are no known reported drug interactions.

Do not give Prospan® to children under 2 years without medical considerations.

Pregnancy and lactation: There are no published studies to establish safety or rationale for the use of Prospan® during pregnancy, or while breastfeeding, so use is not recommended.

Vegetarian and vegan friendly formulas. No added:

- Dairy
- Egg
- Soy
- Yeast
- Sesame
- Peanuts or tree nuts
- Genetically modified ingredients
- Nature identical colours, flavours or sweeteners

References

1. Schaefer A, et al. Efficacy of two dosing schemes of a liquid containing ivy leaves dry extract EA 575 versus placebo in the treatment of acute bronchitis in adults. ERJ Open Res 2019;5:00019-2019. **2. Fazio S** et al. Tolerance, safety and efficacy of *hedera helix* extract in inflammatory bronchial diseases under clinical practice conditions: a prospective, open, multicentre postmarketing study in 9657 patients. Phytomedicine 2009;16:17-24. **3. Schaefer A**, et al. A randomised, controlled, double-blind, multi-multi-centre trial to evaluate the efficacy and safety of a liquid containing ivy leaves dry extract (EA 575®) vs. placebo in the treatment of adults with acute cough. Pharmazie 2016;71:504–9. **4. Lang C**, et al. Ivy in everyday paediatric use: administration of EA 575® to schoolchildren for the treatment of acute bronchitis. Zeitschrift für Phytotherapie 2015;36(05):192-6. **5. European Medicines Agency**. European Union herbal monograph on Hedera helix L., folium. Final. Committee on Herbal Medicinal Products (HMPC) EMA/HMPC/325716/2017.https://www.ema.europa.eu/en/documents/herbal-monograph/final-european-union-herbal-monograph-hedera-helix-l-folium-revision-2_en.pdf**6. Kraft K**. Tolerability of dried ivy leaf extract in children. Zeitschrift für Phytotherapie 2004; 25:179-81 **7.Schlenger R**. Mechanism of action of ivy extract deciphered. Deutsche Apotheker Zeitung 2003;143(49) [translation] **8. Runkel F**, et al. An article on the mechanism of action of ivy. Pharm Ztg 2005;150. **9. Schulte-Michels J**, et al. Mechanism of action of the antiinflammatory properties of EA 575 (Prospan®). Inflammopharmacology 2018, doi: 10.1007/s10787-018-0494-9.