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The beneficial effect of resin-like material made by bees (European propolis hydroalcoholic extract) on the first symptoms (sore throat, muffled dysphonia, and swelling and redness of throat) of mild bacterial and viral infections of the upper respiratory tract

Submission date	Recruitment status	[_] Prospectively registered
21/03/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/03/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
19/11/2020	Respiratory	

Plain English summary of protocol

Background and study aim
The effects of cold and flu on the mouth, throat, and windpipe (upper respiratory tract infections) are very common and are one of the most frequent causes of the doctor's consultation.
Propolis (also known as bee resin) is the generic name used to identify a natural, resinous substance collected by bees (Apis mellifera) from buds and exudates of different plant species consisting of resin (50%), waxes (30%), essential oils (10%), pollen (5%), and other compounds including minerals and organic compounds. Propolis exerts a number of biological properties such as anti-inflammatory and antimicrobial activity. Propolis also has an effect on the respiratory system, as such, it can significantly reduce the number and nocturnal asthma attacks severity. It is able to improve lung function and reduce inflammation defence mechanisms. European propolis hydroalcoholic extract with a high content of polyphenols will be used in the present clinical study to treat mild upper respiratory tract infection.

Who can participate?
Individuals affected by the first symptoms of mild uncomplicated upper respiratory tract infections, aged 18 - 77 years old (updated 05/08/2020, previously: 18 - 65 years old.)

What does the study involve?
Participants are randomly allocated into two experimental groups: placebo and propolis. Treatment: administration (2-4 times/day) of propolis or placebo spray for five days. Participants will be assessed at day three and day five and referred to further treatment if their condition requires it. After 15 days there will be a final assessment.

What are the possible benefits and risks of participating?
Participants taking part in this study should have a benefit on the first symptoms of mild uncomplicated upper respiratory tract infections, including a reduction in the incidence of drug treatment and a reduction in the incidence of the emergence of antibiotic-resistant pathogenic strains. There are no known risks to participants taking part in this study, considering the traditional use of propolis for the maintenance of the oral cavity and upper respiratory tract health.

Where is the study run from?
U.C.C.P (Center for primary care), Benevento (Italy)

When is the study starting and how long is it expected to run for?
December 2019 to January 2020

Who is funding the study?
B Natural (Italy)

Who is the main contact?
Prof. Maria Daglia (scientific), maria.daglia@unina.it
Dr Cristina Esposito (public), cristina.esposito@unina.it

Contact information

Type(s)
Scientific

Contact name
Prof Maria Daglia

ORCID ID
https://orcid.org/0000-0002-4870-7713

Contact details
Università degli Studi di Napoli Federico II
Domenico Montesano street, 49
Naples
Italy
80131
+39 3331703492
maria.daglia@unina.it

Type(s)
Public

Contact name
Dr Cristina Esposito

Contact details
Università degli Studi di Napoli Federico II
Domenico Montesano street, 49
Naples

Italy
80131
+39 (0)81678644
cristina.esposito@unina.it

Additional identifiers

Protocol serial number
PROURTI0119

Study information

Scientific Title
Study of the effect of European propolis hydro-alcoholic extract chemically characterized with high polyphenols content (SPRAY PROPOLIS URTI) on the first symptoms of mild uncomplicated upper respiratory tract infections: a double-blinded, placebo-controlled, parallel-group, single-center study

Acronym
DPRO

Study objectives
The clinical study purpose is to test the propolis extract capacity:
1. To reduce the first common symptoms occurring during mild uncomplicated URTIs and therefore the pharmacological treatment incidence (use of anti-inflammatory and/or antibiotic and/or antitussive drugs)
2. To reduce antibiotic-resistant pathogenic strains incidence at the end of the follow-up, in the subjects in which URTIs is caused by bacteria

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/12/2019, ASL Benevento Ethics Committee (Via Oderisio, n1, 82100, Benevento, Italy; +39 (0)824308419; comitatoetico@aslbenevento1.it), ref: 152869

Primary study design
Interventional

Study design
Interventional double-blind placebo-controlled randomized parallel single-centre trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Uncomplicated mild upper respiratory tract infections

Interventions
Participants are randomly allocated into two experimental groups: placebo and propolis.

t0 (i.e. before the treatment start). Patients with symptoms reflecting a mild uncomplicated upper respiratory tract infection which meet the inclusion criteria are examined for the symptom assessment. The patient is expected to perform the oropharyngeal swab (followed by antibiogram if positive).

Treatment: administration (2-4 times/day) of propolis oral spray or placebo spray for 5 days.

If after 3 days of treatment with propolis or placebo at t1 (3 days after the follow-up visit) fever appears the patient has to be submitted to a visit to evaluate the type of therapeutic treatment to be administered.

If after 5 days of treatment with propolis or placebo at t2 (after 5 days from the start of treatment ie at the end of the treatment) the symptoms and/or fever appears the patient has to be submitted to a visit to evaluate the type of therapeutic treatment administered (the subject is excluded from the clinical trial).

Follow up: t3 monitoring (15 days after the end of propolis or placebo treatment).

The randomization sequence will be generated by a statistician using STATA 16 software (Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC), and subjects (compliant to the inclusion and exclusion criteria) will be assigned to each of the two treatment groups (propoli and placebo) randomly and unpredictably by simple randomization (1:1 allocation ratio). The randomization code will consist of a three-digit number as indicated in the respective Case Report Form (CRF).

Intervention Type
Supplement

Primary outcome(s)
The presence of sore throat, muffled dysphonia and swelling and redness of throat measured by the physician at baseline (t0), t1(after 3 days), t2 (after 5 days)

Key secondary outcome(s)
Bacteria susceptibility test performed at t0 (enrollment time) and t3 (after 15 days).

The Kirby-Bauer method was used to determine susceptibility to antibiotics of the bacteria occurring in the biological material taken from throat swab. The medium used is Mueller-Hinton agar. To prepare the inoculum, 4-5 colonies grown on the primary isolation medium, are suspended in 4-5 ml of Tryptic Soy Broth (enrichment broth), incubating for 2-6 hours.
1. A bacterial suspension adjusted at 0,5 MacFarland standard (see Clinical Laboratory Standards Institute document) is inoculated with a sterile swab on MH agar surface.
2. Antimicrobial-impregnated disks were placed on agar surface, using a sterile tweezers.
3. Plates were incubated at 37°C for 24 hours.
4. Tests were evaluated by diameter alone inhibition around disks.
Reading an antibiogram:
Resistant bacterium: 1 - 9 mm halo
Bacterium with intermediate resistance: 10 - 18 mm halo
Sensitive bacterium: 19 - 30 mm halo

Completion date
20/01/2020

Eligibility

Key inclusion criteria
Current inclusion criteria as of 05/08/2020:
1. Aged 18 - 77 years of age
2. Affected by the first symptoms of mild uncomplicated upper respiratory tract infections

Previous inclusion criteria:
1. Aged 18 - 65 years of age
2. Affected by the first symptoms of mild uncomplicated upper respiratory tract infections

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
122

Key exclusion criteria
1. Individuals with allergies, which could be confused with those with irritation upper airway, object of study
2. Immunocompromised subjects
3. Subjects under immunological therapy
4. Subjects who received antibiotic therapy within 72 hours prior to enrollment
5. Pregnant women
6. Breastfeeding women
7. All patients with overt malignant neoplasia, recent cardio-cerebro-vascular diseases (within 90 days prior to enrollment), with severe middle renal; insufficiency (ascertained with creatinine clearance), and non-autonomous
8. All subjects who according to the doctors are not eligible to participate in the study in question

Date of first enrolment
19/12/2019

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
Italy

Study participating centre
UCCP (Center for primary care)
Via Manzoni, 19
San Giorgio del Sannio
Italy
82100

Sponsor information

Organisation
B Natural

Funder(s)

Funder type
Industry

Funder Name
B Natural

Results and Publications

Individual participant data (IPD) sharing plan
Data of individual patients will be available upon request of patient permission.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	08/10/2020	19/11/2020	Yes	No
Protocol file		26/03/2020	27/03/2020	No	No