SCIENTIFIC EVALUATION FOR AN AUXILIARY MEDICAL DRUG

PROANGI
Spray and throat drops

The request for a SCIENTIFIC EVALUATION for the auxiliary medical drug “PROANGI” spray and throat drops was submitted by the company “APIMELL”, Ohrid, Republic of Macedonia.

Based on the decision of the Scientific Board at the department of preclinical and clinical pharmacology and toxicology at the Medical Faculty in Skopje, I have been assigned to provide a SCIENTIFIC EVALUATION for the auxiliary medical drug “PROANGI” spray and throat drops.

After examining the submitted documentation as well as other relevant information I propose to the Scientific Board at the Institute to accept the following text as a SCIENTIFIC EVALUATION for the auxiliary medical drug “PROANGI” spray and throat drops.
1.0 DESCRIPTION AND CONTENTS

Description: Spray and throat drops

Contents:

100ml solution contains:

- 20 g Propolis dry matter
- essential oils of:
  - Salvia officinalis (Sage) 0.3 g
  - Mentha piperita (Mentha/Mint) 0.6 g
  - Foeniculum vulgare (Fennel) 0.5 g
  - Eucalyptus (Eucalyptus) 0.1 g
  - Menthol (Menthol) 0.3 g
- Alcohol solution ad 100 ml

2.0 GENERAL INFORMATION ABOUT THE DRUG

“PROANGI” spray and throat drops, is an auxiliary medical drug whose function is to alleviate the symptoms of acute and chronic inflammatory processes of the mouth, throat and the esophagus, canker sores, herpes simplex infections, influenza and revalestent conditions, inflammatory processes of the gums and painful abrasions of the mouth.

Proangi is a combination of propolis and essential oils which carry a number of pharmacological properties. The components of Proangi possess bactericidal properties against large number of bacteria(mainly Gram-positive), antiviral properties against( herpes simplex and A2 influenza) as well as anaesthetic and antioxidant properties.

In addition, Proangi successfully removes the unpleasant adour of the mouth.

*Salviae folium*(salvias officinalis-Sage)

Sage(salvia officinalis) is a 30-40 cm tall perennial bush with a pleasant scent. The leaves of the plant (Salviae folium) are picket and used in it’s second year of growth. The leaves are then dried in a cool place with good air circulation or in a driery at 35C.

The drug is composed of 1.5-2.5% essential oil, up to 5% of tannins, a bitter principle called picrosalvina(carnesol) diterpentine compound, flavonoids, resin etc.

The Essential oil(Aetheroleum Salviae) is a clear or yellow-green liquid, with a specific scent and aromatic and bitter flavour.In it’s composition the oil has 50% alpha and beta thujone, about 15% cineol camphor, salvene, borneol etc.
3.0 PHARMACODYNAMICS AND MECHANISMS OF ACTION

"PROANGI" spray and throat drops in it’s composition contain propolis and essential oils well recognized in literature and scientific medicine as compounds which can alleviate the acute inflammatory processes of the mouth, throat, esophagus and ease coughing.

Sage represents one of the oldest plants used in medicine. It is used in the composition of a large number of drugs which are used to wash the mouth and throat in cases of inflammation, due to it’s harmlessness and properties of strengthening the mucosa (due to the action of tannins) and it’s antiseptic properties (due to the action of the essential oil). Due to it’s spasmolytic and anti-inflammatory properties, sage has a positive effect against inflammatory disease of the stomach, intestines, liver, bladder, and the urinary pathways. Sage also helps in patients with diabetes mellitus due to it’s hypoglycaemic properties.

Up until the discovery of antibiotics, sage was used centuries as a tea against sweating in patients with tuberculosis, because, it can reduce the excretion of sweat glands. The drug is also widely used as a spice for grilling meat in the United States because it improves the smell and taste of meat.

Caution should be practised, especially when the essential oil is used because it contains thujone which is a toxic compound.

The essential oil of eucalyptus evaporates easily and is used for inhalations in diseases of the upper respiratory system; usually in combination with menthol and other evaporating substances. The essential oil of eucalyptus has broncholytic, secretolytic and secretomotoric action as a result of which it can ease breathing in diseases of the upper respiratory system.

The main component of the essential oil of mint (Aetheroleum Menthae piperitae) is menthol. Menthol, when applied on the skin and mucus causes a scent of coldness, followed by an easy anaesthetic activity and a pleasant refreshing scent. When used in light concentrations, menthol can inhibit the transport of calcium ions from the thermo-receptors. The sense of coldness is caused because Menthol evaporates easily. It has an antillogistic action. It stimulates the nerve ends of the skin and mucosa. Menthol also has spasmolytic action on the smooth muscle of the intestines; it decreases the transmission of the extra-cellular calcium in the cells.

When applied orally, menthol acts as a holagogue and holoteric. Due to it’s refreshing scent anf flavour, it is often used for improving the flavour of other oral preparates.

In adition, the domesticated mint (Menthae piperitae) has a wide usage both in scientific and home medicine. Mint is a well known spice which has been used for a long time and is quite popular nowadays.

The infusion mint (Mint tea) acts as carminative, stomachic, spasmylytic and a light sedative. It is also used as aholagogum and antidiaroicum due to the presence of tannins in it’s composition.

Due to it’s spasmylytic properties the tea made of mint leaves is a recognized and well appreciated medicament against inflammatory diseases in the stomach and intestines (gastritis, gastroduodenitis, cholitis, peptic ulcerations), flatulence and diarrhea.

Besides that, Mentha piperita stimulates the function of the liver by increasing the production of bladder juice and it’s flow through the bladder canals; it can also aid in the dissolution of bladder stones. This action occurs probably due the presence of menthol and flavonoids. The relaxing properties of mint are also well known; it aids in decreasing and relieve of nervous tension and neurosis.
**Foeniculi vulgare (fennel, Mill)**

The fennel is a biennial plant which can grow up to 1.5 meters. While it's origins lay on the coast of the Mediterranean, this plant is widely grown in many European countries as well as other parts of the world. The fruit of the fennel (*Foeniculi fructus*) has a pleasant scent and aromatic and somewhat spicy taste. The drug from fennel includes 2-6% essential oil, liquid oil 10-20%, protein 16-20%, carbohydrates 4-6% etc. The essential oil (Aetheroleum Foeniculi) is extracted by distillation of squished ripe fennel fruit. It is a clear, colorless or yellow liquid, with a pleasant scent and a bitter-sweet taste. The main component of this oil – anethol (60-89%) consists light doses of: anisaldehyde, anisacetone, anisic acid, fenhon, foeniculin, pinene, camfen, limonene.

**Eucalypti Aetheroleum (essential oil of eucalyptus)**

Essential oil of eucalyptus is obtained by distillation of the leaves and terminal branches of various Eucalyptus types. The main component of the essential oil is cineol (60-80%) (or eucalyptol, cajeputol), besides which, the oil contains: pinenes, camfens, fenhens, various aldehydes, terpineols etc.

**Aetheroleum Menthae piperitae (essential oil of mentha/mint)**

Domestic mynt (Mentha piperita folia) is a perennial zeljesto, branched plant with a pleasant characteristic scent, which can grow from 40-60 in height. Leaves are handpicked from the plant when it's in bloom. The leaves are then dried in a cool place with good air circulation or in a driery at 35 C. Domestic mint contains: 1-3% essential oil, tanines, about 5% flavonoids, bitter substances, ferulic and chlorogenic henna etc. The main component of the essential oil (Aetheroleum Menthae piperitae) is menthol (monocyclic monoterpenic alcohol) which is found in concentrations of 50-68%. 45% of the Menthol is free and 4-12% is esterified with ethanoic acid, isovalerianic and other acids. It also contains ketone-mentone 7-10%, metafuran, therpenes and therpenh derivatives: limonene, cineole etc.

**Propolis**

Propolis is a natural bee product. It is a sappy, yellow-green to dark red substance. By methods of destillation and various solvents it had been determined that propolis contains up to 30% bee wax, about 20% mechanic subcompounds, 40-60% sapp and balsam, 5-10% tannins, pollen etc. However, from a chemical aspect these compounds remain undetermined and it has been proven that the primary components of propolis are the flavonoids which make up to 25% of the propolis composition. The following flavonoids are found in propolis: chrizine, galanine, tectochrizine, acacetin, quercetin and many others. Other then flavonoids, propolis contains significant quantities of minerals, esters of saturated fatty acids, saturated fatty alcohols, 10-15% CarboHydrates, free fatty acids, vitamins etc.
Other than the infusion, the essential oil is used for preparing galenic preparations such as: Aqua, Spiritus, Pastilli, Etoaccharum etc. The essential oil is also added to toothpaste, mouthwash, as an aromatic, deodorant and a desinfectant. It is also used as supplement in various pharmaceutical preparations as well as scent corrector.

**Essential oil of fennel fruit:** Fennel fruit is one of the best supplements for women who are anemic or women who are breastfeeding because it can increase the production of milk. Due to the presence of anethol, the fennel fruit has antiseptic properties. It is used in preparing fomenta which are ten placed on the inflamed or swollen breasts.

In traditional medicine the tea prepared from fennel fruit is very well known and has been in conditions of bad digestion, strengthening the stomach, digestive tract cramps, bad cough and chest pain. Almost all teas and medicaments used against meteorism and similar obstacles in the digestive tract, as well as medicaments used in easing coughing contain fennel fruit. Other than that, fennel fruit has laxative properties as well as antirheumatic properties (when used as a supplement in antirheumatic massage preparations). Due to its pleasant scent ad taste fennel fruit is often used as a corrector both in the pharmaceutical industry as well as in the kitchen.

Propolis has bacteriostatic, bactericidal, and gungicidal properties. The antimicrobial substances is propolis are thermostable. Gram positive bacteria are more sensitive to propolis in comparison with gram negative bacteria. This properties of propolis are mainly due to the action of flavonoids. The propolis flavonoid-acacetin decreases inflammation and increases resistance of the capillary wall. Propolis is used in treatment of various diseases in dentistry, otorhinolaryngology, gastroenterology and diseases of the skin. Propolis has antibacterial, antiseptic, as well as anesthetic and trophic-granular effect which decreases pain and stimulates healing of the wounds.

### 4.0 BENEFITS OF USAGE

“**PROANGI**” spray and throat drops, is an auxiliary medical drug which can alleviate the symptoms of acute chronic inflammatory processes of the mouth, throat and esophagus, aftae, herpes simplex infections, influenza and revalescent conditions, inflammatory processes of the gums and painful erosions of the mouth.

### 5.0 DOSAGE AND USAGE INSTRUCTIONS

*Proangi spray:* 2-3 sprays, 3 times per day, half an hour prior to consumption of food.
*Proangi drops:* up to 30 drops, 3-4 times per day, prior consumption of food.

### 6.0 PRECAUTIONARY MEASURES AND WARNINGS

“**PROANGI**” spray and throat drops are not to be taken by patients sensitive to any of the ingredients of the drug.

*Pregnancy and breastfeeding:* the usage of Proangi should be avoided during pregnancy due to the properties of some of the essential oils which can have an abortive effect and also have an effect on the menstrual cycle.
Notice: The preparate can leave stains on cloth which are difficult to remove.

7.0 PACKING

Proangi spray: 20 ml solution in a spray bottle
Proangi drops: 10 ml solution in a bottle

8.0 STORAGE

To be kept in a dry place on a temperature up to 25C.
TO BE KEPT AT A PLACE WHICH IS NOT ACCESSIBLE TO CHILDREN.

9.0 DATE OF EXPIRY

3 (three) years after date of production. 
Not to be used passed the date of expiry!!

10.0 CONCLUSION

"PROANGI" spray and throat drops, is an auxiliary medical drug which can alleviate the symptoms of acute chronic inflammatory processes of the mouth, throat and esophagus, canker sores, herpes simplex infections, influenza and revalent conditions, inflammatory processes of the gums and painful erosions of the mouth.
Proangi is a combination of propolis and many essential oils, which are recognized in literature and scientifics medicine as substances which can alleviate acute inflammatory processes of the mouth, throat, esophagus as well as ease coughing.
Based on the literature data about the properties and actions of the essential oils which are present in the combination of "PROANGI" spray and throat drops, it can be expected that the drug, or it's components possess the properties which have been attributed by the producer.
Based on everything which has been presented in this SCIENTIFIC STUDY, I conclude that "PROANGI" spray and throat drops – a product made by "APIMELL", Ohrid, Republic of Macedonia, satisfies the auxiliary medical drug conditions in lieu of it's composition and properties, and as such it can be registered in the Republic of Macedonia as an auxiliary medical drug.

The Scientific Study was concluded by
Prof. Dr. Stojmir Petrov
The Scientific Board at the Institute of Preclinical and Clinical Pharmacology and Toxicology, at the meeting held on 18.04.2001 reviewed and approved the scientific evaluation for the auxiliary medical drug "PROANGI" spray and throat drops – a product of the company "APIMELL", Ohrid, Republic of Macedonia.

Director
Prof. Dr. Stojmir Petrov