# THROAT SPRAY SYSTEMS

## Key Considerations When Developing a Throat Spray Solution

By: Degenhard Marx, PhD, and Günter Nadler

### INTRODUCTION

Adults on average suffer from a common cold at least four times every year. Symptoms include headaches, a blocked or runny nose, and often a sore throat. As it's a viral infection, there is no real cure to the common cold; however, symptom relief is a well-established market that commands a great deal of consumer attention, demand, and spending.

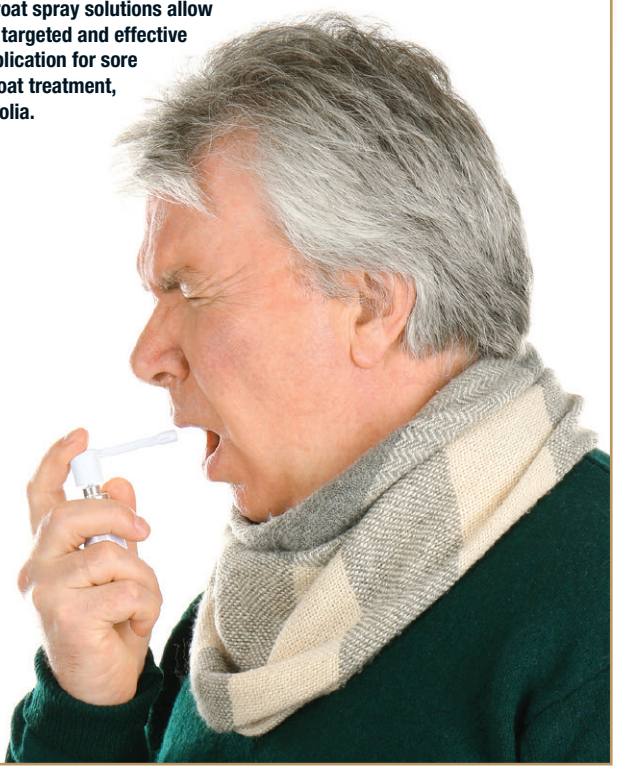
In 2017, more than $8.6 billion was spent over the counter (OTC) for upper respiratory remedies in the US alone, with a further $1.5 billion spent on throat sprays and mouth washes.[1] Although these figures are not for cough and cold treatments alone, as they include remedies for other upper respiratory tract ailments too, they do indicate the scale of the market opportunity. This is further reinforced by data collected in Germany, where in 2017, $1.81 billion was spent on OTC cough and cold medications.[2]

One such opportunity is in throat spray systems. This article will focus on the treatment of sore throats via a pump spray and explore the considerations to be made when developing a reliable spray product.

### REMEDIES RANGE FROM SWEETS TO SPRAYS

The root cause of a sore throat is irritation or inflammation of the throat mucosa. This causes the pain and discomfort, which is worsened by swallowing. The reasons for the irritation or inflammation are varied – they may be viral or bacterial infections, allergic responses, or even snoring. The level of pain, difficulty in swallowing, and the duration of symptoms can be equally varied.

**FIGURE 1**



**Throat spray solutions allow for targeted and effective application for sore throat treatment, Fotolia.**

Just as diverse are the suggested remedies – everything from cold drinks, herbal infusions, and gargling with saline, to lozenges with numbing ingredients.

For relieving mild sore throat symptoms, herbal infusions, cold drinks, or lozenges and candies containing herbal extracts with soothing or numbing ingredients are often the first choice of treatment. However, ingredients in lozenges and candies are released quite slowly and are not always targeted within the oral cavity.

Gargling with saline water, herbal infusions, or other gargling solutions is another often-used therapy to treat sore throat symptoms. Even though gargling is quite effective, it requires a sink and a correct technique for consumers to avoid swallowing part of the gargling solution. Therefore, it is not convenient for on-the-go treatments.

One preferable and convenient, while highly targeted, remedy for a sore throat is the use of a throat spray. With the right actuator, the soft mist dispersed from the throat spray will easily reach the inflamed tissue in the back of the throat to provide fast relief.

A range of different throat sprays are available. Formulations may contain a local anesthetic (eg, lidocaine, benzocaine), an antiseptic (eg, chlorhexidine, cetylpyridinium chloride), herbal extracts, or a combination thereof. Whatever the formulation, it should not contain too much sugar or ethanol, which further irritates the mucosa. And finally, the user should not experience any unpleasant aftertaste.

## THROAT SPRAY TECHNOLOGIES RANGE FROM THE VERY SIMPLE TO THE VERY SOPHISTICATED

The standard for throat sprays is currently a metering pump attached to a bottle containing between 10 to 30 ml of a liquid formulation. The formulation is filled into a glass or plastic bottle with the pump fixed by a screw closure, crimped on or simply snapped onto the bottle neck. Irrespective of the fixing option selected, the system should be tight, with no leakage observed during carrying or handling by the user.

Typically, a throat spray pump will deliver a dose in the range of 50 to 200 µl per actuation. For a targeted administration, the pump will be equipped with an actuator with a prolonged nozzle. The nozzle length may range from 30 to 70 mm. It is easier to target the affected area with such a long-fixed nozzle, but this can be too bulky for users to carry, which is why actuators with foldable or swivel-mounted nozzles were developed.

Less common are devices utilizing continuous valves. A continuous valve delivers a targeted treatment but not precise dosing, as the formulation will be aerosolized while the actuator is pressed down. One technical solution is a tin or aluminum can with pressurized head space. When actuating the valve, the elevated internal pressure will force the formulation out of the can - as long as the valve stem is pressed down. This approach does, however, have some disadvantages, namely that the can does not provide the user with a view of the remaining liquid available for further dosing.

A related but more sophisticated system is the bag-on-valve (BOV) system. In this case, the product is placed inside a bag while a propellant (in most cases just compressed air) is filled in the space between the bag and the outer can. The product is squeezed out of the bag by the compressed air when the continuous valve is actuated. A BOV system will work with any 360 degree orientation. However, the device will not give you an idea of the remaining product.

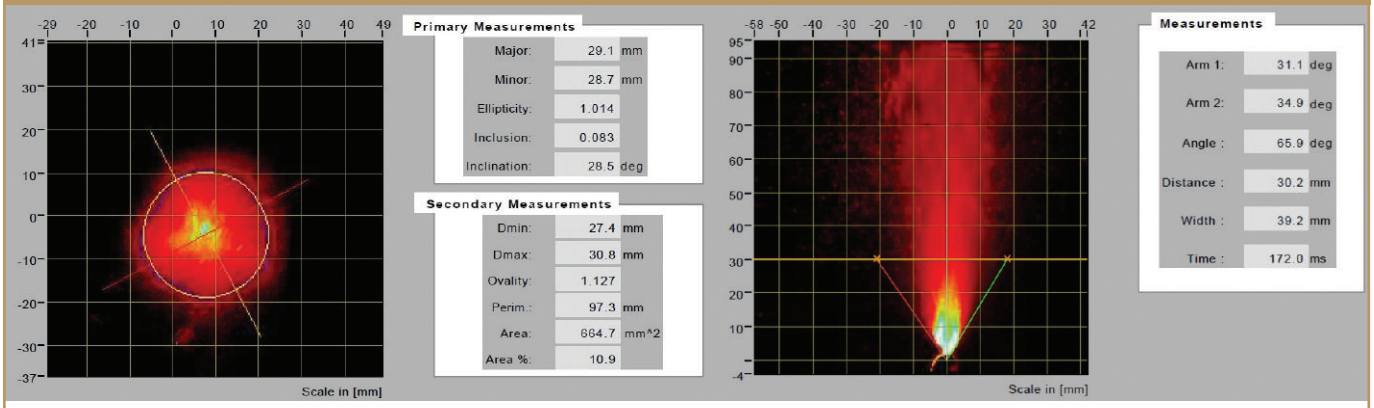
**FIGURE 2**

**Components of a throat spray system.**

**FIGURE 3**

**Actuators with fixed or swiveling nozzles are available.**

## FIGURE 4




**Spray performance tests ensure the formulation's spray pattern and plume geometry is appropriate for the intended use.**

## HOW TO DEVELOP AN APPROPRIATE SORE THROAT REMEDY BASED ON A PUMP SPRAY SYSTEM

### Container Selection is Paramount

Bottles or containers are an integral part of throat spray systems and significantly influence the performance and appearance of the final product. Usually made from glass or plastic, each have their own characteristics, advantages, and disadvantages. Glass has the most obvious disadvantages – it weighs more than plastic and is susceptible to breaking. Critically, the bottle and pump interface must be effectively tested to negate filling line problems and leakages in the final product. Gaskets are often used to ensure perfect tightness between the pump housing and the container. Experienced and expert pump suppliers will be able to recommend a range of fit-for-purpose, reliable quality bottles, whether you are considering a standard or bespoke solution.

### Ensuring the Compatibility of the Delivery System

To ensure the compatibility of the selected system, pump, or valve components and the drug formulation, it is necessary to conduct some basic compatibility testing.

The pump and valve manufacturer will make recommendations based on the necessary mechanical function and to mitigate against the risk of chemical interactions. In practice, potential interactions between the formulation and functional parts due to sorption or swelling cannot be entirely excluded and should therefore be evaluated in an early development stage.

Throat spray formulations may contain ingredients that are very aggressive and can lower the surface tension. This in turn could damage the metal parts and impair the functionality of the pump. Typical tests to mitigate against this include immersion of the functional parts of the pump or valve in the formulation to detect swelling or discoloration. Initial tests with assembled systems from this immersion test will provide insight into the potential effects on mechanical function, such as higher friction, incomplete metering, leakage etc.

A simple test for spray performance will ensure the formulation can be aerosolized by the system and that the delivered spray pattern and particle size is appropriate for the intended use. It is recommended to perform such preliminary compatibility tests with a range of different pumps to establish which can provide the best performance with the given formulation.

### Assessing Performance Characteristics

Spray pattern and droplet size distribution are the most important parameters for the targeted treatment of a sore throat. Spray pattern is a term used to describe the spray angle and the shape of the plume for a fully developed spray. The droplet size is characterized once the spray is fully developed using a laser diffraction method. Fine particles (droplets with less than 10 µm mean dynamic diameter) should be as low as possible to avoid droplet deposition in the lower airways. Regulatory authorities often require characterization of this parameter using a cascade impactor. However, this is an unusual assessment, as the parameter can be easily assessed using a laser diffraction method.

As previously discussed, testing for potential leakage should be done in the early development stage. This ensures that the product integrity is maintained throughout its proposed shelf-life and during use. Exposing the pumps to pressure tests can replicate user behavior and will help prevent complaints from users at a later date. It should be recognized that the manufac-

"Choosing an effective and convenient drug delivery system is key in order to develop brand loyalty for this growing market. The most challenging part of the development process is selecting the correct pump or continuous valve system that will generate a well-defined spray plume with negligible fine particle fraction for the provided formulation."

turers of such pump systems will test the pumps together with some standard bottles using standard media, such as physiological saline. However, it is important to repeat such tests using the actual formulation.

## PREVENTION IS BETTER THAN CURE

People often fear the symptoms and impact of a common cold or upper respiratory infections on daily life, and there are plenty of tips around on how to protect yourself. For example, a Canadian review from 2011 concluded that vitamin C can be recommended to patients for prevention of the common cold (which is not undisputed) and that there is moderate evidence supporting the use of Echinacea purpurea and zinc lozenges for treatment to shorten the duration of the cold.[3]

Another cold prevention solution that often comes in a spray system is zinc, an essential mineral. There have been several studies conducted on zinc as a cold remedy, both in the form of zinc nasal sprays and zinc lozenges, to establish preventive or therapeutic effects. These studies were not able to demonstrate a clear beneficial effect, as the best-run studies found mixed results, but such sprays are still widely used.[3] In June 2009, the US Food and Drug Administration issued a warning statement about intranasal zinc products, available over the counter under the brand name Zicam. The authority stated that zinc nasal gel sprays and other zinc nasal products like swabs may cause permanent or long-lasting damage to the sense of smell. The manufacturer of Zicam products, Matrixx Initiatives, voluntarily withdrew its gel spray and swabs from the market, but later released a reformulated version.

Recently, some carragelose-based nose and throat sprays emerged, claiming protection to virus born upper respiratory infections. For example, the Austrian company Marinomed developed Mavirex, a technology platform based on polymers derived from red seaweed. The first polymer of this platform is Carragelose®, a broadly active anti-viral compound for treating respiratory diseases. The compound prevents the binding of viruses on the mucosal cells, in addition to its moistening effect. There are several nasal, as well as mouth and throat sprays, available and marketed as medical devices with a CE mark in Europe. Yet, these sprays have to be used on a regular basis during the cough and cold season and frequently during the day to have any effect, as the mucociliar clearance will clear the upper airways from the carragelose film. To maintain the optimum protection, the nasal and throat sprays have to be used simultaneously.

There is also evidence that maintaining the mucociliar clearance in the upper airways during the cough and cold season is beneficial, which can be easily done simply by wetting with saline solutions. Consequently, a lot of nasal saline products on the market today are successful. However, for now, there is no device available that has the ability to deliver a reasonable amount of liquid into the nasal cavity and the throat at the same time. This would provide a more effective protection.

Perhaps a type of portable nebulizer with a higher output rate than the conventional ones, and a tuned droplet size for deposition in the upper airways, could be a perfect solution for this task. Breathing through a face mask could then deposit droplets on the mucosa of the whole upper airways. To meet these needs, new technologies would be beneficial as the standard nebulizers are neither portable nor deliver a sufficient output rate for people needing convenience. New technologies could benefit the market, and we look forward to seeing new advances.

## SUMMARY

The potential throat spray market is of considerable size, with peak sales during the cough and cold season. The formulation may contain ingredients that prevent the attraction of a viral infection or to relieve symptoms. The barriers to the development of a throat spray are not particularly high, making throat sprays an attractive delivery method for OTC products, such as sore throat remedies.

Choosing an effective and convenient drug delivery system is key in order to develop brand loyalty for this growing market. The most challenging part of the development process is selecting the correct pump or continuous valve system which will generate a well-defined spray plume with negligible fine particle fraction for the provided formulation.

As throat sprays are most likely used as a quick remedy for symptoms, a foldable nozzle should be considered. Reliable and smooth actuations are mandatory, and any evidence of leakage out of the finished product will represent a significant fail.

To ensure an accelerated and successful product transition from bench to market, it is recommended to establish a development partnership with an experienced pump supplier early on in the process. ◆

## REFERENCES


1. Statistics on OTC use 2017, OTC sales by category, Consumer Healthcare Products Association, March 2018, www.chpa.org/OTCResearch.aspx.
2. The portal for statistics, Statista, Retrieved March 2018, www.statista.com.
3. Nahas R and Balla A. Complementary and alternative medicine for prevention and treatment of the common cold. Can Fam Physician 2011;57:31-36.
4. Allan M and Arroll B. Prevention and treatment of the common cold: making sense of the evidence. CMAJ, February 18, 2014;186(3):190-199.


**To view this issue and all back issues online, please visit www.drug-dev.com.**

## BIOGRAPHIES

**Dr. Degenhard Marx,** following the study of veterinary medicine and the successful completion of his thesis at the University of Leipzig, joined the Arzneimittelwerke Dresden/Asta Medica co-operate research in 1992. In 2001, he took over a senior research position at Altana Pharma/Nycomed in Constance, Germany. During this time in the pharmaceutical industry, he collected ample experiences in the drug development of anti-inflammatory and cardio-vascular drugs. In 2008, he became Business Development Manager at Ing. E. Pfeiffer, Pharma Division, which became Aptar Pharma in 2010. He is now Director Scientific Affairs within the Aptar Pharma Consumer Health Care Division.

**Günter Nadler** is Director Business Development in Aptar Pharma's Consumer Health Care Division. He studied Business Administration and Mechanical Engineering, and started his career at Aptar Pharma 17 years ago in R&D. Before joining the Business Development Team in 2010, he worked in different technical and commercial positions at Aptar Pharma and gained an extensive knowledge of the pharmaceutical drug delivery industry.