

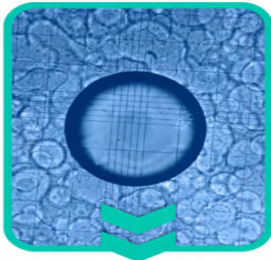


# CREATING A TASTE MASKED AND EASILY SWALLOWED MALARIA DRUG FOR ELDERLY PATIENTS

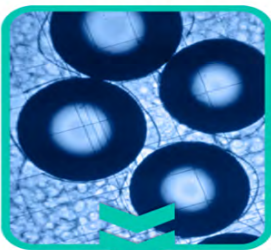


*When a client approached Adare Pharma Solutions with the challenge of creating a taste masked and easily swallowed version of their malaria drug, our experts turned to a custom microencapsulation process for the solution.*

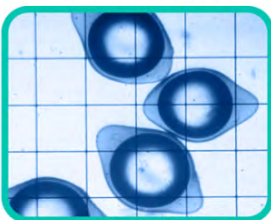
Core and Liquid Coating in Manufacturing Vehicle



Deposition of Liquid Coating Material



Completed Capsules in Manufacturing Vehicle



## THE CHALLENGE

### Hydroxychloroquine, Dysphagia, and Malaria

Hydroxychloroquine Sulfate is most commonly prescribed in tablet form, an easy and convenient way for most patients to achieve compliance. However, there are patient populations that have difficulty swallowing tablets or who can't swallow them at all. Dysphagia, the medical term for difficulty swallowing, can be caused by a variety of factors, including: stroke, head injury, multiple sclerosis, dementia, cancer, or GORD.

Dysphagia often leads to a sharp decline in treatment compliance, since patients will often delay or skip doses of medication to avoid pain or discomfort. In one study, 69% of older patients reported missing or deliberately skipping doses because of their difficulty swallowing.

Dysphagia disproportionately affects the elderly, who are also more susceptible to malaria. A 2003 German study found that not only were the elderly more likely to develop malaria, the effects of the disease on the elderly were far greater than on younger people. A client approached Adare Pharma Solutions with a formulation challenge: create an easily swallowed version of hydroxychloroquine sulfate for the elderly and other patients who suffer from dysphagia.

### Creating An Easily Swallowable Formulation

Most dysphagic patients, when prescribed the tablet form of a medication, are given a compounded formulation, where the tablets are ground into a powder and placed into an inert liquid.

There were major issues with pursuing this strategy with hydroxychloroquine sulfate, however. First, hydroxychloroquine sulfate is extremely bitter, so any compounded version would be very difficult to administer.

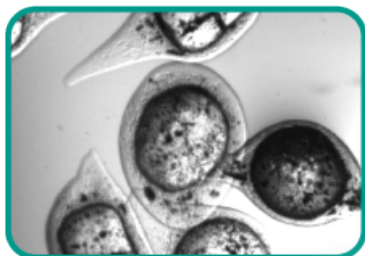
Second, compounded formulations can exhibit significant dosing inconsistencies. A 2006 survey found that 12 of the 36 compounded products surveyed by the FDA failed quality testing, exhibiting potency ranges from 68% up to 268% of the labeled dosage. Both the FDA and the NIOSH list discourage compounded formulations if there are alternatives available. Moreover, our team would need to formulate and taste mask a watersoluble drug, which is often technically difficult.

Our challenge was to formulate a hydroxychloroquine sulfate dosage form that:

- was easy for the elderly and other dysphagic patients to swallow
- was taste masked for easier application
- exhibited consistent and proportional dosing

## THE SOLUTION

After reviewing the goals of the project and the challenges presented by this dosage form, the scientists at Adare Pharma Solutions determined that a microencapsulation process was the most likely candidate for formulation success.



**KCl During  
Micro-Encapsulation**



**KCl Microcapsule  
After Drying**

Microencapsulation encompasses a range of sophisticated drug delivery methods that encloses one or more active ingredient within a protective polymeric material. This technique is often utilized to protect sensitive APIs, achieve taste masking, or to control the release of active materials.

In the patented microencapsulation process developed by Adare, cyclohexane and ethylcellulose are used in a manner that takes advantage of ethylcellulose's ability to dissolve under heat within a cyclohexane-ethylcellulose solution. When cooled, it precipitates out and separates from solution as minute particles that subsequently attach to the surfaces of drug particles to create a uniform barrier membrane. Once the solvent is removed, the result is a free-flowing powder containing microencapsulated API.

For this project, Adare scientists decided that a pre-encapsulation process was needed, one in which hydroxychloroquine was granulated with other excipients as a first step. The resulting granules were then subjected to microencapsulation. Additionally, during development our microencapsulation experts determined that different levels of ethyl cellulose polymer concentration would be most effective in reaching the project's goals.

## THE OUTCOME

The granulated and microencapsulated process we developed successfully created a formulation that met all the challenges of this project. The resulting water-soluble powder is taste masked, easy to swallow, and achieves consistent and proportional dosing.

The hydroxychloroquine sulfate powder can be provided to the patient in convenient single-use sachet form. This powder can be taken by the patient in a variety of ways: it can be administered directly into the mouth, it can be sprinkled over food, and it can be added to water. This flexibility helps add to the convenience factor for this formulation and will hopefully help drive patient adherence.

The microencapsulation technique used here offers other advantages to the project as well. For example, the encapsulated drug can easily be formulated with incompatible API to create multiple-API formulations. Microencapsulation also protects the encapsulated API from moisture and oxygen.

The sponsor of the hydroxychloroquine sulfate project is currently assessing the market feasibility of the product.

Beyond this project, the specific microencapsulation procedures developed for hydroxychloroquine sulfate will be applied to multiple projects involving formulation of a bitter-tasting API, and will be helpful in the development of orally disintegrating tablets for the geriatric and pediatric patient populations.

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## TRANSFORMING DRUG DELIVERY. TRANSFORMING LIVES.

**Adare Pharma Solutions** is a global technology-driven CDMO providing end-to-end integrated services, from product development through commercial manufacturing and packaging, with small molecule expertise focusing on oral dosage forms. Adare's specialized technology platforms provide taste masking, controlled release, solubility enhancement, and patient-centric dosing solutions. With a proven history in drug delivery, Adare has developed and manufactures more than 65 products sold by customers worldwide.

Connect with our experts today: [BusDev@adareps.com](mailto:BusDev@adareps.com)

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