



A Review on Advances in Suppository Technology: Enhancing Bioavailability and Drug Release

Dhatri Sahu¹, Pawan Kumar¹, Tanu Engle¹, Sangeeta Manjhi¹, Pratibha Kanwar¹, Kamini², Harish Sharma³ and Gyanesh Kumar Sahu^{1*}

¹Rungta Institute of Pharmaceutical Sciences and Research, Kohka, Kurud, Bhilai, India

²Rungta Institute of Pharmaceutical Sciences, Kohka, Kurud, Bhilai, India

³School of Pharmacy, Anjaneya University, Raipur, India

*Corresponding Author: Dr. Gyanesh Kumar Sahu, Professor and Dean, Rungta Institute of Pharmaceutical Sciences and Research, Kohka, Kurud, Bhilai, India.

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Gyanesh Kumar Sahu., et al.

Abstract

Suppositories are a widely used pharmaceutical dosage form designed for the administration of medications via the rectum, vagina, or urethra. These solid or semisolid preparations provide an alternative route for drug delivery, especially when oral administration is not feasible due to issues such as gastrointestinal disturbances, swallowing difficulties, or when drugs are poorly absorbed orally. This review provides an overview of the types of suppositories, their formulation, and the various excipients used in their development. It also highlights the advantages and challenges associated with suppository use, including issues related to drug release, patient acceptance, and manufacturing processes. Recent advancements in suppository technology, such as the incorporation of bioavailability-enhancing excipients and the development of novel delivery systems, are also discussed. This review aims to provide a comprehensive understanding of suppositories, their applications, and the current state of research and innovation in this field.

Keywords: Suppositories; Rectum; Dosage Form

Introduction

Although it may not always be the first option, rectal administration of medication is a favored administration due to its greater ease of use and convenience, particularly for the pediatric population. Additionally, when local action is needed, the medication can be used because a high concentration can be reached in the rectum [1-3]. The inferior and middle rectal veins allow some medications that are given low in the rectum to enter the systemic circulation without going via the liver consequently, providing a benefit for medication that are administered orally and undergo first-pass hepatic metabolism medicated solid dosage forms called suppositories are meant to be inserted into bodily orifices (such as the rectum, vagina or urethra) where they will melt, soften or dissolve and have either localized or systemic effects. Suppository volume, shape and consistency make them appropriate for rectal administration. Rectal suppositories are typically torpedo shaped and weigh up to 2g for adults, whereas children suppository weigh approximately 1g [4]. The ability to self-administer suppository suggests that they are simple to use. Additionally, they work well with medication that induce nausea and vomiting such as well as

those that are vulnerable to the stomach unfavorable environment. Suppository can be utilized in targeted delivery system and are show to be appropriate in situations where oral intake is restricted prior to surgery. The inadequate blood supply utilized in a system of tailored distribution [5,6]. The inadequate blood supply cause medications to reach their location of action in the rectum. Activity at a reduced dosage, lowering systemic poisoning but some of the disadvantage of anal or rectal discomfort is a side effect of suppository because insertion, the challenge of self-administration of these doses formed by persons who are physically ill or have arthritis and erratic and fluctuating absorption in vivo in a few example. Suppository can be made by molding them by hand compression and fusion. Control quality suppositories came in both physical and chemical forms [7,8]. Features of the goods, including weight consistency, consistency of texture liquefaction time, melting point, time of melting and solidification, mechanical strength, activity analysis and dissolution test. The study preferred medication, quinine is a cinchona bark derivation methanol quinolone [9]. It is a blood schizonticidal medication that work well against the erythrocytes from each of the four plasmodium species, however it doesn't

affect the formation of exo-erythrocytes. It continues to be utilized in the management of simple malaria in the initial trimester of gestation [10]. In extreme and complex intravenous malaria in children and adults quinine injection are typically advised until oral formulation can be taken by the patient. However, because there aren't enough qualified health staff and lack of access to medical facilities this the administrative path is frequently inapplicable non rural area regions [11,12]. An additional path via regions. The intramuscular method is another way to administer quinine, although it is a common cause of complication in children, including discomfort local inflammation, abscess, tetanus and impairment of the lower extremities [13]. Therefore a different and more practical method of quinine administration is required. In pediatric medicine, the rectal route is frequently employ and evaluate as a substitute for parental administration. Despite its low absorption and early rejection adverse effect, rectal quinine given as an injectable solution or cream has shown promise in treating both simple and promise in treating both simple and complex malaria. The desire to enhance the effectiveness of this other method is driving the development of quinine suppositories, which are more suited to the rectal route enhance its management and adherence [14]. Furthermore, children who are unable to receive oral treatment for moderately severe malaria may benefit from the early management of quinine administration by the rectal route, when has an acceptable safety profile and can prevent the disease from progressing to a severe stage. Rectal formulation of the comparatively less expensive quinine are advised in order to improve early treatment incases of severe malaria, as is usually the cases in rural areas where the disease is frequently endemic therefore, it is necessary to create a stable quinine suppository formulation that is inexpensive, easy to use, and doesn't require any skilled staff or manipulation [15-17].

History

Malaria

Human have been plagued by malaria-like illnesses have been documented for over 5000 years. Malaria induced tertian and quatrain fever was first mentioned in the knee chin about 2700 BCE. In the fourth of medicine, observed the sign of a sickness similar to malaria [18,19]. He also connected Sirius the dog stars appearance to malaria. The Sanskrit medicinal text surtax describes symptoms similar to those of malaria. Malaria was referred to as the king of dossed' in Vedic literature from 1500 to 800 BCE. Neither Aztec nor Mayan literature mention malaria. Malaria may have killed Alexander great. The romans blamed the wetlands for the spread of malaria. Malaria was the true cause of "Roman fever" which afflicted the Roman Empire using DNA- based techniques, it has been established that malaria was common in ancient Egypt circa 800BCE [20]. In order to prevent malaria, the builders of the Egyptian pyramids were give a lot of garlic, according to the ancient Greek his-

torian Herodotus 'The Lleida' by the Greek poet Homer (750BCE) and 'The wasps' by Aristophanes (445-385BCE) both made reference to malaria. Bed nets were employed by pharaoh sneer, who ruled Egypt from 2613 to 2589 BCE, to prevent mosquito bites. The final Egyptian pharaoh, Cleopatra 7, also slept with mosquito nets. Malaria still kills over 600,000 people year and affects about 200 million people, yet researchers have been awarded several Nobel prizes for their work [21,22].

Cinchona bark

It seems that the South American indigenous people were unaware of the therapeutic benefits of cinchona bark, whose bitter flavor made them fearful. The bark was initially employed to treat fevers around 1630 despite peruse discovery in 1513. 'Cinchona' is claimed to have come from a countess of cinchona, the wife of a Peruvian viceroy, who was long thought to have recovered from an illness in 1638 by using the bark. Recent analysis of the counts diary suggests that the countess never experienced malaria or any other fever while she was in Peru, and even though the count did, there is no indication that he was given cinchona bark for treatment [23,24]. In 1639, the remedy- called 'pulvo deal condense' became well known in Spain and gained a significant regulation. The Jesuit priests had a major role in the barks continued distribution, and the narcotic was dubbed Peruvian powder or Jesuits power. The name 'cortex percutaneous' was used when it first appeared in the London pharmacopoeia in 1677 [25]. Originally, the bark was harvested by felling the natural trees, which had been eradicated in many areas. Royal (1839) and Ruiz (1792) proposed growing cinchona in other regions of the world. After wedels seeds sprouted in Paris in 1848, the plants were unsuccessfully brought to Algiers the following year. In 1854, the Dutch made another attempt, bringing seeds and plants into java from Peru thanks to hacker [26,27].

Disease

Malaria

Anopheles insects and vertebrates are both susceptible to malaria, an infections disease spread by mosquitoes. Symptoms of human malaria usually include headaches, nausea, vomiting and fever [28]. In extreme situation it may result in convulsion, jaundice, coma or even death. Ten to fifteen days after being bitten by an infected Anopheles mosquito, symptoms typically appear. People may experience disease recurrences months later if they are not adequately managed. Reinfection typically results in less severe symptoms in people who have just recovered from an infection [29,30]. If the individual is not continuously exposed to malaria, this partial resistance goes away over the course of month to years. Plasmodium infections damage the mosquito vector, reducing its longevity [31,32].

Symptoms

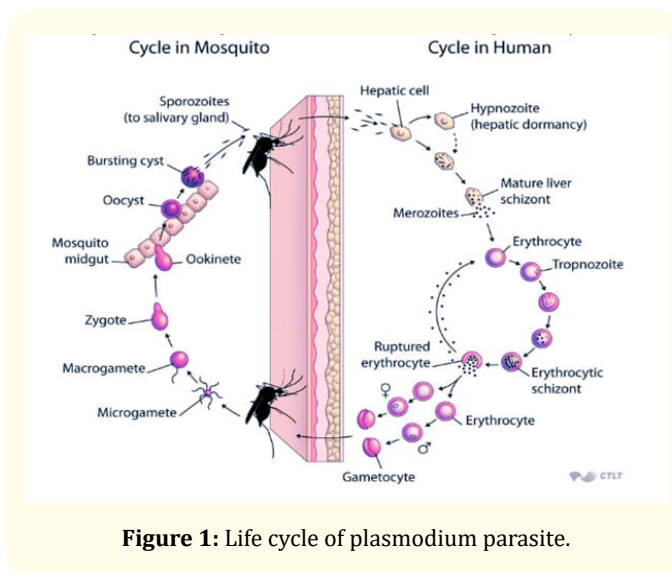
Fever, Chills, Nausea and Vomiting, diarrhea, General feeling of discomfort, Headache, Abdominal pain, Muscle or joint pain, Fatigue, Rapid breathing, Rapid heart rate, Cough [33].

Life cycle

Two hosts are involved in the life cycle of the malaria parasite. A female Anopheles mosquito carrying malaria inoculates the human host with sporozoites during a blood meal. After infecting liver cells, sporozoites develop into schizonts, which burst and release merozoites. (Notably, hypnozoites, a dormant stage in *P. vivax* and *P. ovale*, can remain in the liver for weeks or even years before relapsing and infecting the circulation.) [34]. The parasites replicate asexually in the erythrocytes (erythrocytic schizogony) following this first replication in the liver (exo-erythrocytic schizogony). Red blood cells are infected by merozoites. Trophozoites in the ring stage develop into schizonts, which burst to release merozoites. Certain parasites develop into gametocytes, or sexual erythrocytic stages [35,36]. Clinical signs and symptoms of the disease are caused by blood stage parasites. During a blood meal, an Anopheles mosquito consumes the gametocytes—male (microgametocytes) and female (macrogametocytes). The sporogonic cycle C is the term used to describe the parasites' growth within the mosquito. The microgametes in the mosquito's stomach break through the macrogametes to produce zygotes [37]. The zygotes then develop into elongated, motile ookinetes, which infiltrate the mosquito's midgut wall and mature into oocysts. Sporozoites are released when the oocysts develop, burst, and travel to the mosquito's salivary glands. The malaria life cycle is continued when the sporozoites are injected into a fresh human host [38,39].

Types of plasmodium parasite

- *Plasmodium falciparum* (*P. falciparum*)
- *Plasmodium vivax* (*P. vivax*)
- *Plasmodium Malariae* (*P. malariae*)
- *Plasmodium Ovale* (*P. ovale*)
- *Plasmodium Knowlesi* (*P. Knowlesi*)



Plasmodium falciparum

The most deadly species of plasmodium that causes malaria in human is *plasmodium falciparum*, a unicellular protozoan parasite. The parasite causes falciparum malaria, the most severe form of the disease, and is spread via the bite of a female Anopheles mosquito [40]. About half of all instances of malaria are caused by it. As a result, *P. falciparum* is thought to be the most deadly parasite in human. It is categorized as a group 2A carcinogen and is linked to the development of blood cancer [41].

Plasmodium vivax

Human pathogen *Plasmodium vivax* is a protozoan parasite. The most common and widespread cause of recurrent malaria is this parasite. *Plasmodium vivax* malaria infections can cause serious illness and death, frequently as a result of splenomegaly (a pathologically enlarged spleen), while being less virulent than *Plasmodium falciparum*, the most deadly of the five human malaria parasites. The female Anopheles mosquito carries *P. vivax*; the males do not bite [42,59].

Plasmodium malariae

Human malaria is caused by the parasitic protozoan *Plasmodium malariae*. Along with *Plasmodium falciparum* and *Plasmodium*

vivax, which cause the majority of malarial infections, it is one of numerous types of *Plasmodium parasites* that infect other organisms as pathogens [43]. It is found all throughout the world and produces "benign" malaria, which is not nearly as serious as the kind caused by *P. falciparum* or *P. vivax*. The symptoms include fevers that return roughly every three days, which are longer than the two-day (tertian) intervals of the other malarial parasite and are referred to as quartan fever or quartan malaria [44,45].

Plasmodium ovale

Human tertian malaria is caused by the parasitic protozoon *Plasmodium ovale*. The majority of malaria infections worldwide are caused by *Plasmodium falciparum* and *Plasmodium vivax*, two

of the several kinds of *Plasmodium parasites* that infect people. Compared to these two parasites, *P. ovale* is uncommon and far less harmful than *P. falciparum* [46,60].

Plasmodium knowlesi

Plasmodium ovale is a parasitic protozoon that causes tertian malaria in humans. Two of the several types of *Plasmodium parasites* that infect humans, *Plasmodium falciparum* and *Plasmodium vivax*, are responsible for the bulk of malaria infections globally. *P. ovale* is rare and much less dangerous than *P. falciparum* in comparison to these two parasites [47,48].

Dosage form

S. No.	Brand Name	Type	Dose	Quantity
1	Rez -Q	Capsule/Tablet	100 /300mg	10
2	Rez -Q	Injection	300mg/ml	1ml/2ml
3	Rez -Q	Liquid	NA	60ml
5	A -Quin	Capsule/Tablet	300mg	10
6	Qinarsol-300	Capsule/Tablet	300mg	10
7	Qinarsol -300	Injection	300mg/ml	1ml/2ml
8	Qinarsol 300g	Film coated tablet	300mg	10
9	Quinine	Capsule/Tablet	300mg	10
10	Quinine	Injection	300mg/ml	2ml
11	Quininga	Tablet/Capsule	100/300mg	10
12	Quininga	Injection	300mg/ml	10×2ml
13	Kuinil	Injection	300mg/ml	2ml
14	Quinex	Tablet	300mg	10
15	Kuinil	Capsule/Capsule	300mg	10
16	Cinkona	Capsule/Capsule	100mg/300mg	10
17	Cinkona	Liquid	150mg/5ml	60ml
18	Cinkona	Film Coated tablet	100mg/300mg/600mg	10
19	Queenolar	Capsul/tablet	150mg/300mg	10
20	Queenolar	Injection	300mg/ml	2ml
21	Queenolar	Liquid	50mg/5ml	30ml/60ml
22	Quin-9	Oral suspension	150mg	60ml

Table 1: Dosage form.

New drugs

- Quinine nanoparticles
- Quinine liposomes
- Quinine sublingual
- Quinine buccal
- Quinine inhalable powder
- Quinine injection nanoemulsion

Patent

S. No.	Authors	Title	Patent no.	Submission	Publication	Reference
1	Ping chen, Duncan McVey, Douglas E. Brough, Joseph Bruder	Malaria antigens and methods of use	US10780153B2	2019-04-24	2020-09-22	[49]
2	Stephen Trowell, Amalia Berna, Benjamin Padovan, Vicki Locke	Method of detecting plasmodium infection	US10101319B2	2014-11-28	2018-10-16	[50]
3	Arnab kumar Chatterjee, Advait suresh Nagle, Prasuna Paraselli	Compounds and compositions for the treatment of parasitic diseases	US9926314B2	2016-07-26	2018-03-27	[51]
4	Varun MITTAL	Corpus search system and methods	US10372739B2	2018-09-07	2019-08-06	[52]
5	Robert A. Levine, Michael B. Jorgensen	Method and apparatus for detecting the presence of intraerythrocytic parasites	US9046473B2	2012-09-28	2015-06-02	[53]
6	Joseph Joel pollak, Daniel Levner, Yonatan bilu	Method and systems for detecting entities in a biological sample	US11584950B2	2019-12-06	2023-02-21	[54]
7	Emil P. Kartalov, Aditya Rajagopal, Axel Scherer	Signal encoding and decoding in multiplexed biochemical assays	US11866768B2	2020-07-23	2024-01-09	[55]
8	Liangfang Zhang, Che-ming jack Hu	Nanoparticles leverage biological membranes to target pathogens for disease treatment and diagnosis	US10285952B2	2016-01-19	2019-05-14	[56]
9	Aydogan Ozcan, Onur Mudanyali, Stoyan Dimitrov, Uzair Sikora	Portable rapid diagnostic test reader and methods of using the same	US10663466B2	2014-10-31	2020-05-26	[57]
10	Matthew R. Behrend, Michael C. Hegg, Matthew P. Horning, Benjamin K. Wilson	Systems, devices and methods including a dark-field reflected illumination apparatus	US8774884B2	2011-01-10	2014-07-08	[58]

Table 2: Patent.

Future prospects

- **Improved bioavailability:** Quinine suppositories can be designed to absorb quinine more quickly and efficiently.
- **Targeted delivery:** Quinine suppositories can be designed for targeted delivery, delivering quinine directly to the affected area.
- **Increased patient compliance:** Patient compliance can be increased by making quinine suppositories easy and comfortable.
- **Reduce side effect:** Quinine suppositories may be designed to reduce the side effects of quinine.
- **New indications:** Quinine suppositories may be explored for new indications, such as in cancer treatment.
- **Pediatric use:** Quinine suppositories may be designed for pediatric use, making quinine accessible and effective in children.

- **Geriatric use:** Quinine suppositories may be designed for geriatric use, allowing quinine to be administered with ease and effectiveness in elderly patients.
- **Combination therapy:** Quinine suppositories may be designed for combination therapy, allowing quinine to be used with other medications.

Conclusion

Quinine suppository is a new and innovative dosage form that helps the body absorb Quinine quickly and more. Its future prospects include improved bioavailability, targeted delivery, increased patient compliance, reduced side effects, new indications, pediatric use, geriatric use, and combination therapy.

While designing and developing the Quinine suppository it is important to keep in mind its safety, efficacy, and quality. After this, it can be launched in the market and provide a new and better treatment option to the patients.

The conclusion of Quinine suppository is that it is a new and innovative dosage form that helps in absorbing Quinine quickly and more in the body. Its future prospects are very promising and it can provide a new and better treatment option to the patients.

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