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Sustained release of medications in liquid form: utility, advantages, and disadvantages

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ABSTRACT

Dosage forms function as vehicles for delivering drugs into the body, with oral formulations typically classified as solid, liquid, or gaseous. Among these, liquid oral dosage forms are often preferred due to their superior bioavailability relatively to solids ones, as well as their enhanced absorption and ease of administration. These formulations are prepared by dissolving or suspending active pharmaceutical ingredients in suitable solvents. Key challenges in liquid formulations – such as taste masking, dose uniformity, and excipient optimization (e.g. sweeteners and viscosity modifiers) – are critical for ensuring patient acceptability and effective drug delivery. Modified-release dosage forms (including controlled-release, extended-release, delayed-release, and sustained-release systems) are designed to improve therapeutic outcomes by enabling prolonged drug delivery, reducing dosing frequency, and minimizing side effects. Sustained-release drug delivery systems are particularly beneficial in chronic conditions such as hypertension, where continuous medication is required. These systems aim at maintaining consistent plasma drug concentrations while attenuating peak levels to reduce the risk of toxicity. The ideal sustained-release formulation would support a single-dose regimen that delivers therapeutic effects over days, weeks, or longer. Several systems (such as diffusion-, dissolution-, and osmotic pressure-controlled systems) have been developed in order to achieve sustained release. However, challenges remain, including incomplete drug release, the risk of dose dumping, and the need to maintain therapeutic drug concentrations in a consistent manner.

1. Introduction

Dosage forms (including oral solids, liquids, gases, inhalers, granules, and tablets) are employed in order to administer drugs *via* routes

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such as oral, topical, rectal, and ophthalmic. These forms vary between infants and adults, with mechanisms of action tailored to individual physiological and therapeutic needs. Sustained-release systems, including controlled-release and depot formulations, aim at prolonging therapeutic effects, reducing dosing frequency, and minimizing side effects by delivering drugs uniformly over time. Liquid preparations, which typically offer superior bioavailability, face challenges such as taste masking and dose uniformity. These issues are often addressed using excipients including sweeteners and viscosity modifiers. Recent advancements (e.g. the development of nanoparticles, microparticles, and transdermal patches) have improved drug bioavailability and reduced adverse effects, with polymeric microparticles emerging as a promising delivery platform[1,2].

The development of sustained-release drug delivery systems seeks to enhance drug efficacy by reducing the number of doses or by localizing delivery at the site of action, thereby minimizing the required dosage while ensuring uniform distribution. An ideal drug delivery system meets two key conditions: it provides a single dose with a treatment period ranging from several days to a week, as in infectious diseases, or it enables lifelong therapy, as in chronic conditions such as hypertension and diabetes. This short review highlights the importance of sustained-release drug systems in improving drug efficacy and patient compliance compared to immediate-release formulations.

2. Problems that occur during multiple dosing

If the dosing interval does not correspond to the biological half-life of the drug, plasma concentrations may fluctuate outside the therapeutic range, potentially resulting in toxicity. Such variability is inconvenient for patients and may contribute to missed doses and poor adherence to the prescribed regimen[3].

3. Modified-release dosage forms

Modified-release formulations are designed to alter the release profile of a drug compared to conventional dosage forms. The drug release may be delayed or extended, depending on the desired therapeutic effect[4].

4. Categories of modified-release dosage forms

Controlled-release formulations release the drug at a constant rate, thereby maintaining relatively stable plasma concentrations over time. Extended-release drugs are taken less frequently than their immediate-release counterparts. For example, controlled-release metformin (Glucophage XR), used in the treatment of type 2 diabetes, provides a gradual release of metformin throughout the day, helping maintain stable blood glucose levels. Controlled-release medications (including sustained-release and long-acting formulations) are designed to provide a continuous drug supply over prolonged periods. In order to avoid rapid absorption, the design must mitigate excessively high peak plasma concentrations. An example is prolonged-release diltiazem (Cardizem CD); a calcium channel blocker that delivers the drug slowly for extended blood pressure control.

Delayed-release preparations postpone the release of the active ingredient for a specific time after administration. Examples include repeat-acting tablets and capsules, as well as enteric-coated tablets that utilize barrier coatings in order to delay release. Delayed-release omeprazole (Prilosec), a proton pump inhibitor used for the treatment of gastro-oesophageal reflux disease, exemplifies this category by releasing the drug in the small intestine, thereby avoiding gastric degradation.

Sustained-release drugs maintain steady plasma levels by releasing the drug at a controlled rate over an extended period, thus minimizing side effects. The primary goal of sustained-release systems is to improve patient compliance while enhancing bioavailability and therapeutic efficacy[1,5].

5. Advantages of the sustained-release drug delivery system

Sustained-release systems enhance patient conven-

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ience and adherence by lowering dosing frequency. They also minimize fluctuations in drug plasma levels, resulting in improved disease control and fewer adverse effects. For high-potency drugs, precise management of plasma concentrations increases safety and optimizes drug utilization, potentially reducing total dosage requirements. Furthermore, these systems help contain healthcare costs by shortening treatment durations, limiting the need for frequent dosing, and reducing the time and the resources required for administration and monitoring[6].

6. Disadvantages of the sustained-release drug delivery system

Limitations of sustained-release systems include incomplete drug release, increased first-pass metabolism, chemical instability, and insufficient residence time in the gastrointestinal tract for the achievement of full absorption. Additionally, discrepancies between *in vitro* and *in vivo* behaviour can affect predictability. Patient behaviours (such as chewing oral drugs or altering food intake) may cause dose dumping, thereby increasing the risk of toxicity. Moreover, in overdose situations, the recovery of sustained-release drugs can be particularly difficult[7,8].

7. Approaches to a sustained-release drug delivery system

Various advanced strategies have been developed in order to improve therapeutic performance and patient compliance. Diffusion-controlled systems regulate drug release through polymer barriers, enabling consistent and predictable delivery. Dissolution-controlled systems base release on the rate at which the drug dissolves. Combining both approaches results in hybrid systems that optimize release profiles through simultaneous dissolution and diffusion mechanisms. Furthermore, ion exchange resin–drug complexes facilitate tailored drug interactions, thereby enhancing release characteristics. Finally, pH-dependent formulations[9] exploit gastrointestinal pH gradients for targeted drug release, while osmotic pressure-controlled systems[4] rely on osmotic principles in order to ensure regulated medication delivery over time.

In controlled diffusion-release systems, the diffusion of dissolved drug molecules through a polymer barrier is the rate-limiting step. As the insoluble matrix gradually depletes, the diffusion path lengthens, preventing zero-order release kinetics. Controlled-release technologies typically depend on diffusion through polymeric membranes[6], and can achieve programmable delivery by fine-tuning formulation and processing parameters[10].

8. Conclusion

Sustained-release liquid dosage forms represent a significant advancement in drug delivery, offering solutions to critical challenges related to patient compliance and therapeutic reliability. Modified-release systems, including sustained-release formulations, improve clinical outcomes by maintaining consistent drug levels in the body over extended durations, thereby minimizing dosing frequency, and reducing the risk of side effects or toxicity associated with peak plasma concentrations.

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Conflicts of interest

None exist.

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