



Oral modified-release dosage forms: A terminological challenge in science and regulatory affairs

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ABSTRACT

Solid oral modified-release dosage forms (SOMRDFs) are pharmaceutical technologies that alter the rate and/or onset of drug release compared with immediate-release (IR) formulations. This has been a significant advance, as many IR formulations fail to reach or maintain therapeutic plasma concentrations for the required duration to treat diseases, primarily due to the problematic biopharmaceutical and pharmacokinetic characteristics of many active ingredients. Types of SOMRDFs are described by regulatory entities in the USA as extended-release and delayed-release. However, research in the literature and other regulatory entities does not apply consistent criteria regarding the terms used to name these types of formulations. This review shows that the terminology used for SOMRDFs is frequently not associated with specific characteristics of dissolution profiles. The use of confusing terms in the brand names of products with SOMRDFs in Colombia was also identified. This significant conceptual misunderstanding could lead to errors in the prescribing and use of these technologies and could mislead future researchers investigating this field. The purpose of this review is to minimize future misinterpretations when referring to or researching any type of modified release technology by proposing harmonized terms for describing SOMRDFs.

1. INTRODUCTION

Oral administration is one of the most studied and widely used strategies for systemic drug delivery in many therapeutic areas. It employs a wide range of dosage forms due to its convenience, non-invasive approach, and patient compliance [1]. Many drugs act by maintaining stable, safe, and effective concentrations in the bloodstream for the required duration. Achieving this therapeutic goal requires the careful design of dosage forms that ensure adequate drug release rates and absorption profiles, along with proper medical prescription and patient adherence [2].

Most drugs can be administered through an immediate-release (IR) dosage form without major inconvenience to follow a treatment at prescribed time intervals according to medical instructions. However, due to their chemical nature, some drugs have inherent risks when they are orally administered, whether because of their limited solubility, permeability, instability under physiological conditions, or risk of toxicity due to accumulation in organs and tissues; hence, they are restricted by narrow therapeutic windows. Several decades ago, it was discovered that a strategy to solve this problem was the use of modified drug delivery systems, as they can improve pharmacotherapy by maintaining therapeutic plasma concentrations, reducing dosing frequency, and improving adherence to the pharmacological treatment [3].

Solid oral modified-release dosage forms (SOMRDFs) are classified in two main categories: Delayed-release (DR) and extended-release (ER) [4]. However, the definitions and terminology used for subtypes of SOMRDFs are not consistently standardized among health authorities and researchers worldwide [5,6]. Oral ER formulations can be found in scientific literature

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and official documents referred to as sustained-release (SR), prolonged-release (PR), controlled-release (CR), timed-release, repeated-release, programmed-release, “long-acting”, “repeat action”, “prolonged-action”, and “ultra-long acting” products. This suggests that different terms may reflect differences in drug release characteristics, or that they are sometimes used arbitrarily, creating ambiguity and hindering a comprehensive understanding of this subject.

Unlike other studies that address the description of specific aspects of modified drug delivery systems, this research focuses on compiling and analyzing information from articles and books in recognized databases, as well as from technical documents issued by the main regulatory authorities across the Americas, regarding terms, concepts, and definitions applicable in these territories for SOMRDFs. As a result, this review clarifies relevant terms and classifications, which can help both the academic and professional health community, as well as non-experts in the health field, to better understand and appropriately apply the terminology related to these health technologies.

2. MATERIALS AND METHODS

2.1. Data sources

This research was conducted using as primary resources original research articles available in the databases ScienceDirect, Springer, PubMed, Taylor & Francis, and Google Scholar.

The literature search was performed using the combinations of the keywords [“Drug modified release (MR)” OR “Drug delivery system” OR “Modified release”] AND “Oral” (quotation marks included), in title and abstract, and restricted to complete scientific articles (excluding conferences, letters, lectures, abstracts, or other type of documents). The last date of search was March 26, 2025.

Scientific review articles and books were used as secondary sources, identified by using the databases and keywords mentioned before. For books, the database Access Pharmacy was also included.

In addition to the research articles and books, official documents from regulatory health authorities in the Americas were also reviewed to identify the definitions and classification of oral MR formulations. These authorities included the Colombian National Food and Drug Surveillance Institute (Instituto Nacional de Vigilancia de Medicamentos y Alimentos, INVIMA); the Peruvian General Directorate of Medicines, Supplies and Drugs (Dirección General de Medicamentos, Insumos y Drogas); the Ecuadorian National Agency for Regulation, Control and Sanitary Surveillance (Agencia Nacional de Regulación, Control y Vigilancia Sanitaria, ARCSA); the Argentinian National Administration of Drugs, Foods and Medical Devices (Administración Nacional de Medicamentos, Alimentos y Tecnología Médica); the Chilean Public Health Institute (Instituto de Salud Pública de Chile); the Paraguayan National Directorate of Sanitary Surveillance (Dirección Nacional de Vigilancia Sanitaria); the Uruguayan Ministry of Public Health—Medicines Division (Ministerio de Salud Pública, División de Medicamentos); the Brazilian Health

Regulatory Agency (Agência Nacional de Vigilância Sanitária, ANVISA); and the U.S. Food and Drug Administration (FDA).

Official national pharmaceutical compendia in the Americas were also consulted, including the Argentinian, Brazilian, Mexican, and United States pharmacopoeias. The official documents were located by targeted searches directly on the official websites of the health authorities, accessed through Google, or directly in the compendia, looking for MR-associated content.

The INVIMA (Colombia) platform was accessed to review the “Unique Medicines Code [Código Único de Medicamentos (CUM)]” report as of June 2025, to compare the pharmaceutical forms assigned by INVIMA with the brand names of each product. For this purpose, the database was filtered in the pharmaceutical-form field using the words “liberación” and “entérica”.

2.2. Studies selection

The reports from scientific databases were selected following the PRISMA flow diagram presented in Figure 1 [7]. The inclusion criteria were:

- Articles from 2010 to 2024, except those presenting definitions of the different types of oral drug release, for which no time restriction was considered.
- Articles published before 2010 authored by researchers with Hirsch index (H) ≥ 10 [8], verified using Web of Science Journal Citation Reports (JCRs) [9].
- Articles published in English, Spanish, and Portuguese.
- Articles from journals with an impact factor ≥ 2.3 , according to the Web of Science JCR [9].
- Articles presenting definitions for SOMRDFs or *in vitro/in vivo* studies related to SOMRDFs.
- Books published between 2020 and 2024 contribute definitions for SOMRDFs.

Exclusion criteria included:

- Reports referring to conventional drug release or administration routes other than oral.
- As a quality assessment criterion, original articles that do not provide experimental data supporting the type of oral release, such as *in vitro* dissolution profile, mathematical release models, or drug plasma concentration–time profiles, and those with a lack of coherence between methods and results.

These criteria were manually verified during screening and eligibility assessments.

A total of 4,693 records were initially identified, but 3,199 were removed early, mainly for being duplicates, which were identified using Zotero [10]. The remaining 1,492 records were screened by titles and abstracts, leading to the exclusion of 986 for not meeting the predefined inclusion and exclusion criteria. A second screening was performed by an independent researcher, and discrepancies were resolved by consensus with the participation of the lead researcher; this process resulted in the exclusion of 945 records and left 547 available for full-text reading. Quality assessment was applied to these reports, leading to the exclusion of 401, which resulted in 146 studies included in this research (Fig. 1). Dual review was also applied in all stages of the assessment.

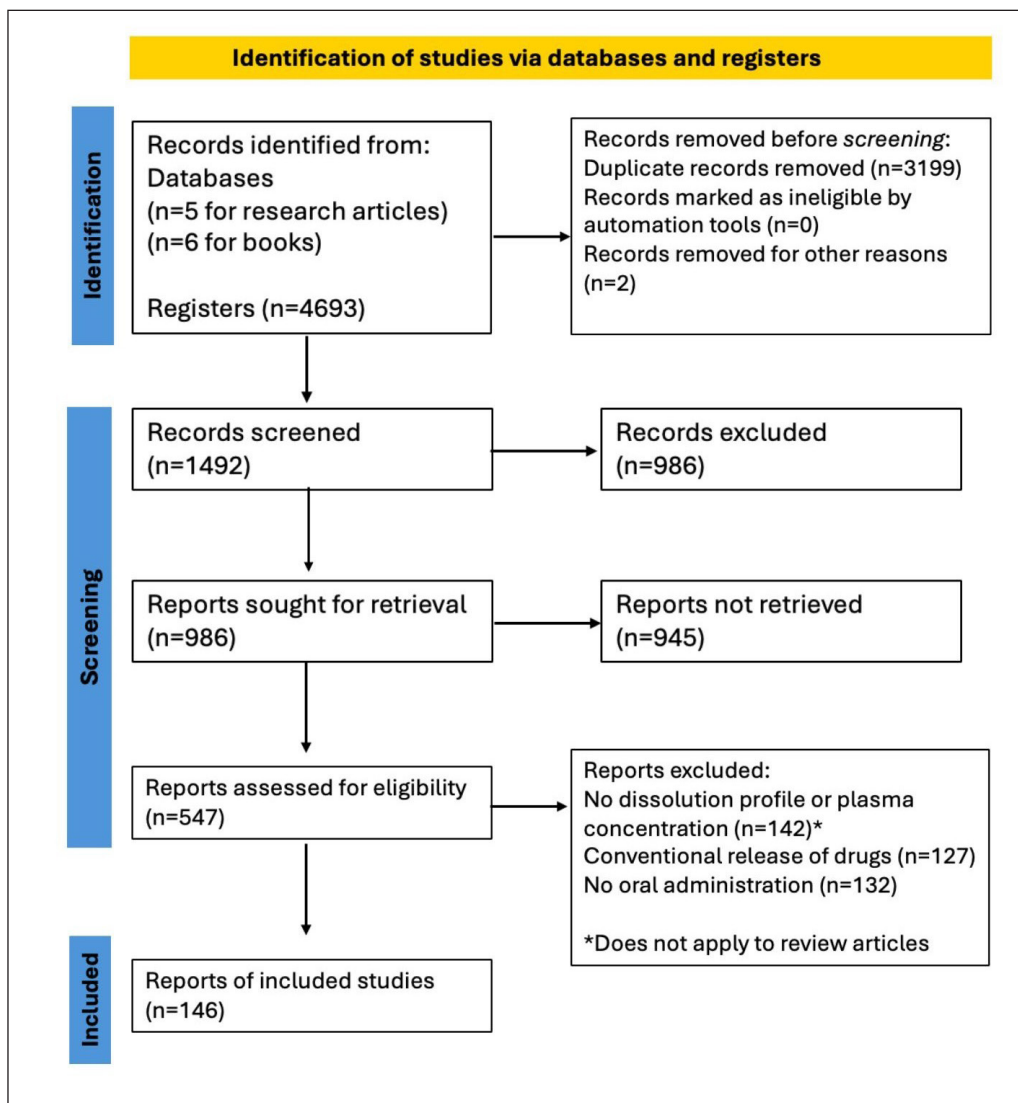


Figure 1. PRISMA flow diagram of the research.

2.3. Data extraction

From review articles, books, official documents, and compendia, terminology and definitions associated with SOMRDFs were extracted.

From original articles presenting *in vitro/in vivo* studies related to SOMRDFs, the following variables were collected: time of onset release, time to maximum release, maximum percentage released, and the mathematical model and/or technology used. For articles evaluating multiple formulations, only variables from the formulation identified by the authors as preferred were considered. Where the preference was not mentioned, the variables from all formulations were collected as a range. When data were not reported or could not be reliably extracted from graphs, the variable was marked as “no data”.

The extracted information was transferred to a Microsoft Excel [11] data matrix that also included the document title, authors, year, methods (where applicable), and

data collected. The transfer of information was also subjected to dual review.

Original articles presenting ER formulations were grouped based on the SOMRDFs terminology cited, and variables were presented as the range of the grouped values or as the maximum reported, when applicable.

3. RESULTS

3.1. Terms associated with SOMRDFs according to health authorities in the Americas

Since special delivery technologies emerged, health authorities worldwide have needed to define and classify the different types of oral MR dosage forms. In this section, a compilation of such definitions by health authorities in the Americas is presented, organized chronologically and by institution.

In 1990, the United States Pharmacopeia (USP) defined MR pharmaceutical forms and their drug release characteristics—such as timing and/or location—as those designed to achieve therapeutic goals or provide convenience not possible with conventional formulations. The USP classified these systems into three categories:

- ER dosage forms: Those that release a dose allowing a twofold reduction in the frequency of administration when compared to an IR dosage form.

- DR dosage forms: Those that release discrete portions of the drug at times other than immediately after administration, although a fraction may be rapidly released conventionally. Enteric-coated dosage forms are the most common DR products.

- Targeted-release dosage forms: Those that release the drug at or near the site of desired physiological action and may have immediate or ER features [12].

Over time, the USP discontinued the term “targeted-release” as an official category, and the designation of MR was limited to two main types, ER and DR, as the terms used in official article titles. Throughout the different editions of the USP, equivalent terminology for these definitions has been gradually recognized. In the USP 30 NF 25 (2007), the terms SR, CR, and “prolonged-action” were cited as equivalents of ER [13]. By 2018, the USP 41 NF 36 acknowledged “repeat action” as another equivalent for ER dosage forms [14], and in 2019, the USP 42 NF 37 introduced “long-acting” as an additional synonym [15]. Meanwhile, for DR dosage forms, the expressions “enteric coated” and “gastro-resistant formulations” have been used over time by USP to describe formulations in which drug release is prevented in the stomach but promoted in the intestine.

The current USP (2025) definition of MR no longer refers to the site of drug release but rather focuses on its rate and timing, indicating that these parameters are altered compared to IR products. ER no longer implies a twofold reduction in the frequency of administration compared to an IR dosage form, but instead refers to formulations specifically designed to prolong drug release regardless of the dosing frequency [4].

In 1997, the FDA published the guidance document “SUPAC-MR: MR Solid Oral Dosage Forms”. In this document, MR dosage forms were classified into two types:

- ER: Products formulated to make the drug available over an extended period after ingestion, allowing a reduction in dosing frequency compared with a drug presented as a conventional dosage form (e.g., as a solution or an IR dosage form).

- DR: Products that release a drug (or drugs) at a time other than immediately following oral administration [16].

Years later, in 2014, the FDA guidance “Bioavailability and Bioequivalence Studies Submitted in NDAs or INDs—General Considerations” stated that MR products include both ER (equivalent to CR and SR) and DR formulations. Although DR products are defined as MR dosage forms, the document notes that many behave like IR products once the intended delay has elapsed [17]. The 2022 version of this guidance maintains the same classification [18].

In 2007, the Oriental Republic of Uruguay, through Decree No. 12/007 (Official Gazette No. 27.165-A), approved technical recommendations for bioequivalence studies (*Aprobación de las recomendaciones técnicas para la realización de estudios de bioequivalencia contenidas en el documento Intercambiabilidad de medicamentos*), classifying MR systems into PR and DR. For the former, it was stated that they release the drug over a longer period after administration than IR forms, without any reference to a reduction in the frequency of administration. For DR products, it was highlighted that the onset of drug release is postponed until the product passes through the stomach due to an enteric coat, after which it behaves as an IR formulation [19].

The Brazilian Health Regulatory Agency (ANVISA) published the 5th edition of its pharmacopeia in 2010. In volume I, MR dosage forms were classified into two categories: PR and DR. Although ANVISA did not provide a general definition for MR formulations, it preferred the term PR over ER, and did not adopt alternative terms—such as SR, CR, or “repeat action”—commonly used by the USP and FDA.

According to ANVISA, PR refers to formulations that enable at least one reduction in dosing frequency compared with conventional forms. Additionally, DR formulations are defined as those resulting from a specific design or manufacturing method that postpones the release of the active substance. Gastro-resistant preparations are also considered a type of DR by ANVISA [20].

In Volume I of the 7th edition of the 2024 Brazilian Pharmacopeia, the same classification and definitions of MR formulations (PR and DR) were maintained, reaffirming that PR formulations are designed to achieve at least one reduction in dosing frequency compared to conventional dosage forms [21].

In 2013, the Republic of Costa Rica, through Decree No. 32470-S, “Technical Guide for the Application of Post-Registration Changes in Medicines with Therapeutic Equivalence (*Guía Técnica para la Aplicación de Cambios Post-Registro en Medicamentos con Equivalencia Terapéutica*)”, described MR dosage forms as pharmaceutical preparations in which the rate and/or site of drug release differs from that of conventional dosage forms. This modification is achieved through a particular formulation design or a special manufacturing method. MR dosage forms include “PR”, “enteric”, “pulsatile” release, and others. The definitions provided in this guide are detailed below:

- CR: A term that describes, without precision, the release of the active ingredient from any formulation designed to follow a predetermined kinetic release profile.

- PR: A formulation that does not release the total dose of the active pharmaceutical ingredient (API) immediately after administration but instead does so slowly enough to extend the dosing interval two or more times, with no initial fast dose.

- Repeated release: The API is released at time intervals, and plasma concentrations are similar to those of a conventional release dosage in each one.

- SR: A formulation that allows the rapid release of a fraction of API in the initial phase, followed by a gradual release of the remainder for a prolonged time, thereby minimizing high plasma concentration fluctuations [22].

Unlike what is observed in other entities, the Costa Rican guideline is the only one that explicitly distinguishes between PR and SR, based on the presence or absence of an initial rapid release. The Chilean Institute of Public Health, later, in 2018, presented the same classification as Costa Rica in its “MOVAL 01” guide [23].

The 7th edition, volume IV of the 2013 version of the Argentinian Pharmacopoeia explains that expressions such as “prolonged action”, “extended action”, and SR are regularly used to describe pharmaceutical forms. However, PR is encouraged to be used for official titles. Regarding DR forms, it specifies that they delay the release of the API until after it has passed through the stomach, which is again referred to as enteric-coated formulations. This version of the Argentinian pharmacopoeia remains in use [24].

The Ministry of Health and Social Protection of Colombia (MSPSC), along with the INVIMA, through Resolution 1,124 of 2016, established that MR products include both ER and DR dosage forms, and that ER are indistinctly known as CR, PR, and SR dosage forms. In this resolution, no formal definitions are suggested for any of the SOMRDFs [25].

In 2018, the guide “Studies on Bioequivalence of Solid Oral MR Medicines (*Estudios de Bioequivalencia de medicamentos sólidos orales de liberación modificada*)”, which is originally referenced in the norm NOM-177-SSA1-2013 [26] and released General Health Council of Mexico (Consejo de Salubridad General, CSG) of the United Mexican States, also stated that MR pharmaceutical forms are formulations in which the rate and/or the site of drug release differs from that of oral IR forms.

The definitions are as follows:

– DR: A condition in which the formulation allows for a delay in the release of the API, including gastro-resistant products. Key characteristics related to DR products include: the release of the drug occurs sometime after administration; the formulation is resistant to gastric fluids; once release begins, the formulation behaves as an IR form; there is only a delay in achieving measurable plasma concentration without extending the overall duration of the therapeutic effect; the formulations are usually coated or pH-dependent and are intended to delay release until the drug reaches the absorption site, where the pH allows its release.

– PR: A pharmaceutical form designed to make the active ingredient bioavailable for a longer period after its administration. In this system, it is mentioned that there are more types, such as “SR”, “ER”, “CR”, and “repeated” releases, but no explanation or distinction among these subtypes is provided. However, this guide affirms that there is no harmonization of terms used to describe the different systems of SOMRDFs; nevertheless, the classification is presented as an enunciative and non-limiting approach [27].

In the same year, 2018, Health Canada released the guidance document “Comparative Bioavailability Standards: Formulations Used for Systemic Effects” and defined MR dosage forms as drug formulations that differ from conventional products in the rate at which the drug is released.

No classification is provided in the document (e.g., ER or DR), focusing instead on describing the different objectives that these formulations may have, such as delaying disintegration or dissolution, providing effective drug concentrations for a longer time, minimizing gastrointestinal or other adverse effects, reducing fluctuations in drug concentrations, and producing multiple peaks and troughs in the concentration-time profile after a single administration (i.e., multiphasic MR dosage forms) [28].

The Republic of Paraguay, through Resolution S.G. N-092 of 2020, established a classification of MR dosage forms into PR and DR. For PR, it is stated that it can also be called CR, although no complete definition is provided. Meanwhile, for DR, the resolution refers to formulations with gastro-resistant coating, which suggests that drug release is delayed until the product reaches the intestine [29].

The Republic of Ecuador follows the same classification as the Colombian government in the Resolution “ARCSA-de-2024-038-DASP” issued in 2024, maintaining ER and DR as the main categories for MR dosage forms [30].

In Figure 2, a summary is presented of the terms used to classify the SOMRDFs as provided by the different health authorities across the Americas.

Over the years, the classification of MR pharmaceutical forms has remained largely consistent across regulatory entities. These authorities have also recognized the different terminologies used in literature and by marketing authorization holders (MAHs) as equivalent terms. However, two principal types are generally recommended: DR and ER (referred to as PR in most Spanish-speaking countries), which emphasize, respectively, the delay in the onset of release and the prolongation of the duration of the release to reduce dosage frequency. This consensus has been addressed through the evolution of USP definitions [1990–2025] [4,12–15], the classification from the FDA [1997–2022] [16–18], and those from Uruguay (2007) [19], Colombia (2016) [25], Mexico (2016) [26,27], Canada [28], Paraguay (2020) [29], Brazil [2010–2024] [20,21], and Ecuador (2024) [30].

3.2. Terms associated with SOMRDFs according to authors publishing in scientific journals

This section reviews the classification and definitions of the different types of SOMRDFs reported by authors in scientific articles and textbooks, selected according to the criteria described in the methods section.

In 1984, De Haan and Lerk [31] described and used CR as a collective term for any formulation in which the release rate is altered through galenic manipulations. They also agreed that oral drug products providing a longer duration of pharmacological effect are classified as SR, “prolonged acting”, and/or “repeat action” drugs. It is notable that instead of using the term “release” they chose “action” to classify some types of SOMRDFs. The authors indicated that there are slight differences between “prolonged acting” and SR preparations, but these were not clarified in the document. It was stated that it is challenging to classify products in these categories, and therefore, both terms are used interchangeably [31].



Figure 2. Summary of terms used by health authorities in the Americas to classify SOMRDFs.

Later, in 1995, Buckley *et al.* [32] used the term CR to cover various methods that allow modification of drug release and therefore absorption, including transdermal administration products and oral preparations with “slow-release”, ER, and DR. Although the different types of release were not explicitly defined by the authors, it was reported that ER products maintain plasma concentrations for a longer time than “slow-release” products [32].

In 2002, Suñé [5], highlighted that the terminology used to define the SOMRDFs is broad and confusing, a point that motivated the present review. Nevertheless, the author presented several categories, each with a specific definition:

- SR forms: initially release enough drug to achieve the desired pharmacological response rapidly and subsequently release an adequate and constant quantity of drug to maintain the absorption rate equal to the elimination rate for a period, usually 10 to 24 hours. Therefore, these pharmaceutical forms

exhibit zero-order release kinetics, resulting in constant plasma drug concentrations.

- ER forms: correspond to those formulations in which the drug is initially released in an amount sufficient to produce a therapeutic action or even in a small excess that is never harmful to the organism, followed by a slower release but at a rate that is not always equal to that for elimination. In other words, these pharmaceutical forms present a slow but non-constant release, producing plasma concentrations that fluctuate within the therapeutic zone, describing a wide curve.

- Repeated release forms: provide an initial dose of the drug and later release another similar dose.

- DR forms: release the API after a latency time, so that plasma levels of the drug remain zero until it reaches a specific region of the gastrointestinal tract where the release occurs [5].

As observed above, for this author, both SR and ER forms include an initial release phase, but SR aims to maintain constant plasma concentrations, whereas ER allows controlled fluctuations in plasma levels over time.

In 2015, a review by Patel and Patel [33] classified MR dosage forms into several categories, including ER, SR, DR, CR, “repeat action”, “prolonged-action”, and targeted-release. These dosage forms refer to products that alter the timing and rate of drug release. This text highlights some characteristics of each of them, as follows:

- ER forms: reduce the dosing frequency compared with IR forms.
- CR forms: enable a slow release of the drug over an extended period, but it is not possible to determine a precise release rate.
- SR forms: provide a specific and measurable delivery rate for an extended period.
- Prolonged-action forms: release the drug slowly and provide a continuous supply of the drug over an extended period.
- Repeat action forms: deliver a first dose, followed by a second release at a later time.
- DR forms: release a discrete portion of the drug at a different time after administration, although a small portion may be released immediately.
- Targeted-release forms: release the drug at or near the intended site of action, and may exhibit ER characteristics [33].

Based on these definitions, it can be interpreted that ER and CR are general classifications for SOMRDFs, while PR and SR are categories assigned to those where the rate of drug release is specifically determined.

In 2020, Trenfield and Basit [34] adopted the classification proposed by the USP in 1983, which includes ER, DR, and targeted-release. ER is described as providing at least a twofold reduction in dosing frequency compared with an IR product. Examples of this type of release include SR, CR, and “long-acting” formulations. DR products are described as releasing discrete portions of the drug at specific times after administration, without an explicit reference to a latency period. According to these authors, targeted-release may also behave as an IR product after the administration; examples include gastroretentive devices and colonic drug delivery systems [34]. As mentioned previously, the current USP does not consider targeted-release as part of SOMRDFs.

In 2022, Ducharme *et al.* [35] aligned with the classification and definitions proposed by Trenfield and Basit [34] for SOMRDFs, with some distinctions. The term “time-release drug products” was included as an equivalent to ER products. Gastroretentive devices and colonic drug delivery systems were excluded as examples of targeted-release products, and another type of SOMRDF was incorporated by the authors, the orally disintegrating tablets (ODTs). These are defined as formulations in which the drug is dispersed in saliva and swallowed with little or no water [35]. Notably, no other author in this review included this pharmaceutical form within the SOMRDFs categories. Likewise, neither the USP nor the FDA classifies ODTs as SOMRDFs [36].

In 2022, Soares *et al.* [37] defined PR as those formulations designed to release the drug more slowly than IR products, typically resulting in a long plasma concentration plateau period [37]. This definition is consistent with that proposed by Patel and Patel [33] for prolonged-action forms. No additional SOMRDFs definitions were reported by Costa *et al.* [37].

In 2024, Pather [6] recommended using only the terms ER (administered once or twice a day) and DR (referring to a lag time before release) and suggested that other terms and acronyms should be avoided when describing SOMRDFs. The author highlighted that alternative terms, such as SR, PR, CR, and timed-release, have been widely and interchangeably used for marketing purposes, and even though efforts have been made to standardize their use, this has led to confusion about what they actually mean [6]. Similar concerns have been raised by other authorities and authors, including the CSG from Mexico (2016) [26,27] and De Haan and Lerk [31].

In the same year, Kir, *et al.* [38] described CR products as formulations designed to prolong the therapeutic effect, maintain constant drug concentrations within the therapeutic range, reduce dosing frequency, minimize adverse effects, and improve patient compliance. The authors also emphasized that crushing SOMRDFs may compromise these therapeutic goals [38]. This definition is more comprehensive, as it incorporates clinical considerations and aligns with the descriptions provided by other authors for SR dosage forms by referring to a constant drug concentration. No other definitions of SOMRDFs were included in the publication.

Among authors, it is difficult to identify a clear consensus regarding a unified classification or consistent definitions of SOMRDFs. Researchers use a wide range of terms, often with overlapping or ambiguous distinctions, and some publications even propose using all these terms indistinctly. Moreover, a notable difference is observed compared with health authorities: the preference for the term “action” (e.g., “prolonged-action”) instead of “release”, which appears to refer not only to the duration of drug release but also the resulting duration of the therapeutic effect. In addition, the use of the term targeted-release is inconsistent with health authorities, who have already ceased to recommend it.

The arbitrary use of these terms creates confusion and hinders understanding for students, professors, and other stakeholders. A call to address this situation and simplify the terminology is necessary to prevent misinterpretation.

3.3. Use of terminology in research of SOMRDFs

This section reviews the use of the terms related to SOMRDFs in original research from different authors, analyzing dissolution profiles, plasma concentration curves, and other characteristics associated with these terms to identify inconsistencies or trends in terminology usage.

Out of 137 articles reviewed, 62 used the term “SR”, 37 used “CR”, 19 used “prolonged-action”, 10 used “DR”, 2 used “MR”, 5 used “ER”, 1 used the term “Ultra-long acting”, and 1 reported “Slow release”.

For most of the DR products (8 of 10 reports), the findings were consistent with definitions provided by health authorities and other authors. Initial release times ranged from 15 to over 180 minutes, while the maximum drug release varied from 65% to 100%, occurring between 120 and 720 minutes, depending on the formulation composition and the type of polymer used to modulate release. However, two articles described formulations with an immediate onset of release that were stated as DR products.

Table 1 summarizes the variability in onset and extent of drug release across DR formulations.

For oral ER dosage forms and their alternative terms (127 reports), most formulations exhibited an immediate onset of release, although some showed release beginning between 25 and 270 minutes after drug administration. The maximum percentage of drug released varied widely depending on the formulation, pH, polymers, and other factors, ranging from low (<10%) to high (>80%) release. The time to reach the maximum release is a key parameter for properly describing the release behaviour of any drug [38]; a broad range of times was observed across studies, from 120 to 12,000 minutes. Kinetic models were infrequently reported, being provided in only 58 of 127 reports. The zero-order, first-order, Higuchi, and Korsmeyer–Peppas models were the most applied for ER formulations. Additionally, 36 reports indicated the presence of a burst release phase.

Table 2 summarizes the characteristics of ER formulations, including those reported under alternative terminology. Overall, no distinctive features were identified among the different terms, suggesting that they are often used arbitrarily and could be used interchangeably.

According to the health authorities from Costa Rica [22] and Instituto de Salud Pública de Chile [23], and the author Suárez (2002) [5], two specific characteristics are expected for SR dosage forms, as a special type of SOMRDF: to exhibit an initial burst release and to follow zero-order kinetics. However, only 19 out of 62 reports (31%) indicated a burst release, and only 5 reported zero-order release kinetics. Among other terms for SOMRDFs, 12% of the reports specified an initial burst release, and 10% stated zero-order kinetics. These findings support the conclusion that the term

SR cannot be considered exclusively associated with these release behaviors.

The analysis of dissolution profiles from the reviewed reports led to the identification of cases where an initial burst release was not explicitly indicated but could be inferred from the data. For this evaluation, burst release was considered when two distinct release phases were observed in the profiles, with the initial phase related to the faster dissolution of the drug molecules [39]. Fourteen reports (23%) using the term SR were identified as exhibiting a burst release based on profile evaluation. Taking into consideration these reports together with the previously reported 31%, a total of 54% of the times that the term SR was used were associated with a burst release effect, while 46% neither mentioned nor exhibited this behaviour. A similar analysis was applied to reports using other SOMRDFs terminology; in this case, 41% of the reports appeared to present an initial burst release; when combined with the previously reported 12%, a total of 53% of the cases using terms other than “SR” were also associated with burst release. These findings reinforce the conclusion that the terminology used for SOMRDFs is often applied arbitrarily, and that SR is not consistently used as a distinct category of SOMRDF but rather as an equivalent term to “extended” and “prolonged”, as recognized by most health authorities.

To this stage of the review, the terminology proposed by health authorities appears clearer and more concise than that used by researchers, likely reflecting different objectives and contexts. For regulatory purposes, kinetic characteristics are not used as criteria for defining SOMRDFs; rather, the key factors are the onset and extent of drug release. In contrast, researchers tend to be more specific, showing interest in characterizing the effect of formulation variables on the drug release profile, which has led to the introduction of additional and sometimes redundant terms to refer to SOMRDFs. In our understanding, this lack of alignment may create confusion among healthcare professionals, patients, and students in chemistry and health sciences. Therefore, it is important for researchers and regulatory authorities to work together to establish harmonized terminology for SOMRDFs that promotes clarity, improves communication, and minimizes misinterpretation.

Table 1. Characteristics of DR formulations, according to the literature reports reviewed.

Onset of release time (min)	Maximum percentage released	Time to maximum release (min)	Technology used	Reference (s)
180	90	420	Surelease (ethyl cellulose)	[40]
30–120	80–99	120–720	Methacrylic Acid Copolymer (Eudragit® L100-55)	[41]
90	100	180	Hydroxypropyl methylcellulose phthalate (HPMCP), polyvinyl alcohol, glucomannan and, polyethylene glycol 600	[42]
75	81	480	Hydroxypropyl methylcellulose K15M, Carbopol 934P and, polyvinylpyrrolidone K30	[43]
120	65–100	180–480	Eudragit® and poly (ethylene oxide), polyvinylpyrrolidone and, lactose monohydrate	[44]
120	85–100	169	Stearic acid (SA) pellets through hot melt extrusion	[45]
105–120	100	155	Microcrystalline cellulose (MCC) (Avicel PH-101), alginic acid, dextrin pellets through granulation, extrusion and spherization	[45]
15–30	100	150	Polyvinyl alcohol (PVA) and polylactic acid (PLA) filaments 3D-Printed Gastro-Retentive Floating Device (tablets)	[47]

Table 2. Characteristics of ER formulations, according to the literature reports reviewed.

Dosage form terminology cited	Onset of release time (min)	Maximum percentage released	Time to maximum release (min)	Mathematical model reported	Reference(s)
PR	Immediate	15–100	180–4,320	Higuchi, Local regression, Korsmeyer-Peppas model, Brunauer-Emmett-Teller, Zero-order, First-order, Hixson-Crowell	[48–66]
CR	Immediate 60–120	30–100	300–4,320	First-order, Bi-exponential Zero-order, Weibull model, Monolag, Higuchi, Hixson-Crowell, Korsmeyer-Peppas	[38, 67–100]
SR	Immediate 25–180	10–100	120–12,000	Power law, Hixson-Crowell, Zero-order, First-order, Higuchi, Korsmeyer-Peppas	[101–140,47, 141–158]
ER	Immediate	80–100	210–1,440	No data	[159–162]
Ultra-long-acting	Immediate	12–28	20,160	No data	[163]
CR and DR	Immediate	No data	1,440	No data	[164]
Modified-slow release	Immediate	No data	150–174	No data	[165]
MR	210–270	No data	1,440	No data	[166]
SR and CR	Immediate 120	76–100	300–4,320	No data	[167, 168]
Diffusion CR	Immediate	20–55	360–720	No data	[169, 170]
ER and SR	Immediate	14–55	360–4,320	No data	[171]
Slow-release	Immediate	60–80	1,440	No data	[172]
DR	Immediate	20–85	2,880	No data	[173]

PR: Prolonged-release, CR: Controlled-release, SR: Sustained-release, ER: Extended-release, MR: Modified-release, DR: delayed-release (named as it by the cited authors). Overall, most ER formulations exhibit an immediate onset of release, wide variability in extent of release, and diverse kinetic models, suggesting that ER terminology is associated with the intent to prolong drug release and/or its clinical effect, rather than a specific dissolution pattern.

3.4. Terminology used by the regulatory authority and MAHs for the SOMRDFs in Colombia: case study

This section reviews the terminology employed by the Colombian regulatory authority (INVIMA) and by MAHs for SOMRDFs, using data from the “Unique Medicines Code (CUM)” database [174]. The analysis considered marketing authorization records that are currently valid, undergoing renewal, or temporarily suspended.

As of June 2025, there were 3,791 authorizations classified as some type of SOMRDFs by INVIMA. In general, this authority uses the terms “PR” and “DR”, consistent with the descriptions provided in the prior section. As mentioned in section 3.2, Resolution 1,124 of 2016 from the MSPSC suggested the use of the term “ER” for formulations that release the drug over a longer period than conventional products. Nevertheless, “prolonged”, which is the term most frequently used by INVIMA in the CUM database, is accepted as an equivalent designation under this regulation [25].

Remarkably, the term “enteric coated”, which, according to our review, corresponds to a type of DR dosage form, was used by INVIMA 72 times ($\approx 1.9\%$). Additionally, nine records ($\approx 0.2\%$) used the term “MR” as the pharmaceutical form without further specification of the type of modification, including records of marketing authorizations approved in 2025. This lack of specificity may create ambiguity in the interpretation of the dosage form for healthcare professionals, pharmacists, and patients.

Regarding MAHs, a variety of terms were identified in commercial product names to indicate the type of release: “PR”

(46 times $\approx 1.2\%$), “DR” (36 times $\approx 0.9\%$), the expression “retard” (36 times $\approx 0.9\%$), “MR” (4 times $\approx 0.1\%$), “CR” (3 times $\approx 0.08\%$), and “programmed-release” (2 times $\approx 0.05\%$). The remaining 3,583 products ($\approx 94.5\%$) did not include any reference to the type of release in their names. Interestingly, 18 products, including the expression “retard”, which is a word semantically related to “delayed”, were assigned by INVIMA the pharmaceutical form “PR”, whereas 15 other products named “retard” were not classified as SOMRDFs by the authority.

It was also observed that 23 products containing the expression “DR” in their brand name were classified by INVIMA as IR pharmaceutical forms, such as coated tablets or hard capsules. Similarly, one product labelled “PR granules” was not categorized as a SOMRDF in the CUM database.

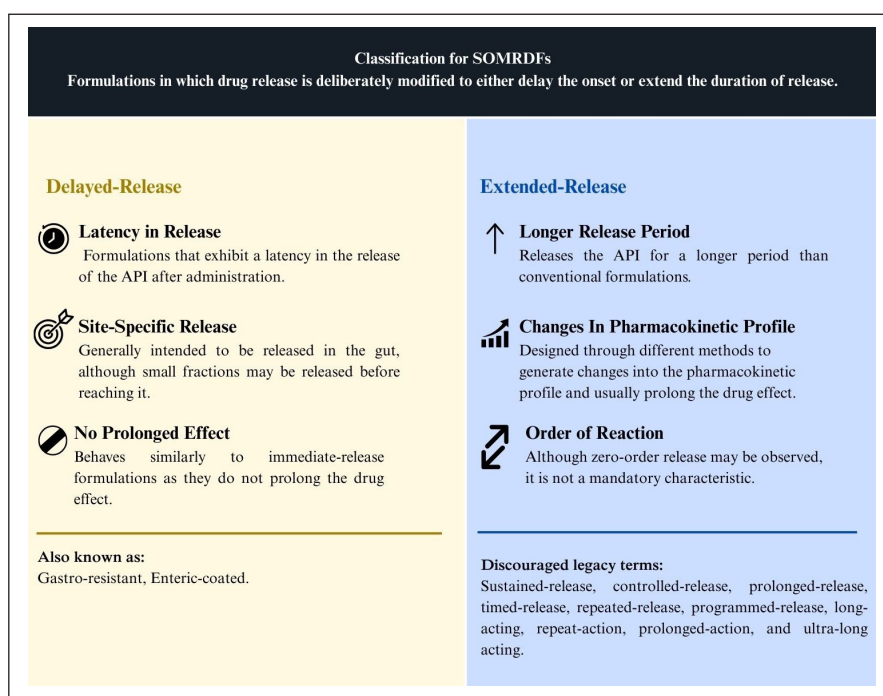
In Table 3, a summary of inconsistencies found within the SOMRDFs report from INVIMA is presented.

These findings underscore the inconsistency and indiscriminate use of terminology to name products within the industry and highlight the need for regulatory measures to ensure alignment between product naming and official classification of the pharmaceutical form. Furthermore, it is recommended that the regulatory authority in Colombia mandates labelling requirements to include the drug release type in the packaging of the product to minimize the risk of misinterpretation by prescribers and patients. This is particularly relevant when IR versions of the same API are also available, as misinterpretation could lead to prescribing or dispensing errors and potentially compromise patient safety.

Table 3. Summary of inconsistencies between product naming and regulatory classification.

Product name	Pharmaceutical form according to health authority	<i>n</i>
Expression DR included	Not classified as MR	23
Expression “retard” included	PR or SR tablets	18
Expression “retard” included	Coated tablet without any reference to MR	15
Expression “XR” included	Unclassified	5
No type of MR included	Referred as MR without any type of specification	5
Expression PR included	Not classified as MR	3
Expression MR included	Referred as MR without any type of specification	2
Expression PR included	Referred as MR without any type of specification	2

Source: database “Código Único de Medicamentos” from Colombian National Food and Drug Surveillance Institute (Instituto Nacional de Vigilancia de Medicamentos y Alimentos, INVIMA), report as of June 2025.

**Figure 3.** Harmonized classification of SOMRDFs.

4. CONCLUSION

After a comprehensive review of information from health authorities in the Americas, research worldwide, reports from marketing authorization databases, and information from MAHs, the need for a harmonized terminology for SOMRDFs is reaffirmed. As a contribution to clarifying this matter, the following definitions and classification of terms for SOMRDFs are proposed:

Oral MR dosage forms: Formulations in which drug release is deliberately modified to either delay the onset or extend the duration of release.

– DR: Formulations that exhibit a latency in the release of the API after administration. They are generally intended for intestinal release, although a small fraction may be released before reaching the gut. These products behave similarly to IR formulations, as they do not prolong the drug

effect. They are also known as gastro-resistant and enteric-coated formulations.

– ER: Formulations that release the API over a longer period than IR products. They use a variety of technological approaches to alter the pharmacokinetic profile of the drug and usually prolong the drug effect. Although zero-order release may be observed, it is not a mandatory characteristic. The following are discouraged legacy terms, rather than separated categories: “SR”, “CR”, “PR”, “timed-release”, “repeated-release”, and “programmed-release”.

Terms referring to “action” instead of “release” are strongly unsupported and should be avoided (e.g., “long-acting”, “repeat-action”, “prolonged-action”, and “ultra-long acting”).

Figure 3 provides a visual summary of the proposed classification of SOMRDFs resulting from this review.

5. LIMITATIONS

The review was limited by the search criteria (databases, keywords, and period included) and by the timing of the search. The review of documents from health authorities and compendia was limited to those from the Americas.

6. AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

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8. CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

9. ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

10. DATA AVAILABILITY

All data generated and analyzed are included in this research article.

11. PUBLISHER'S NOTE

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REFERENCES

- Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in oral drug delivery. *Front Pharmacol.* 2021;12(1):1. doi: <http://doi.org/10.3389/fphar.2021.618411>
- Stielow M, Witczyńska A, Kubryń N, Fijałkowski Ł, Nowaczyk J, Nowaczyk A. The bioavailability of drugs—the current state of knowledge. *Molecules.* 2023;28(24):19. doi: <http://doi.org/10.3390/molecules28248038>
- Boyd BJ, Bergström CAS, Vinarov Z, Kuentz M, Brouwers J, Augustijns P, *et al.* Successful oral delivery of poorly water-soluble drugs both depends on the intraluminal behavior of drugs and of appropriate advanced drug delivery systems. *Eur J Pharm Sci.* 2019;137:104967. doi: <https://doi.org/10.1016/j.ejps.2019.104967>
- United States Pharmacopeial Convention. The United States pharmacopeia—national formulary (USP-NF 2025). Rockville, MD: The United States Pharmacopeial Convention Inc.; 2025.
- Suñé J. Nuevas aportaciones galénicas a las formas de administración. In: *Fundación ProMedic. Barcelona: real Academia de Farmacia de Cataluña. Barcelona, Spain; 2002.*
- Pather I. Modified-release oral dosage forms. In: Weitz M, Boyle P, editors. *Pharmaceutics for pharmacy students.* New York, NY: McGraw Hill; 2024.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Br Med J.* 2021;372(71):32. doi: <http://doi.org/https://doi.org/10.1136/bmj.n71>
- Luque A, Román P. La producción científica de los químicos españoles y el índice h de Hirsch. *Quím.* 2006;102(2):11–7. doi: [https://doi.org/10.1016/S1697-2600\(14\)70050-X](https://doi.org/10.1016/S1697-2600(14)70050-X).
- Web of Sciences. [Internet]. London, UK: Clarivate; 2024. Available from: doi: <https://clarivate.com/academia-government/scientific-and-academic-research/research-discovery-and-referencing/web-of-science/>
- Zotero [Software]. Version 7.0.24. Fairfax (VA), USA: Corporation for Digital Scholarship; 2024. Available from: <https://www.zotero.org/>.
- Microsoft Excel [Software]. Redmond (WA): Microsoft Corporation; 2025. Available from: <https://office.microsoft.com/excel>
- Cohen JL, Hubert BB, Leeson LJ, Rhodes CT, Robinson JR, Roseman TJ, *et al.* The development of USP dissolution and drug release standards. *Pharm Res.* 1990;7(10):983–7. doi: <http://doi.org/10.1023/a:1015922629207>
- United States Pharmacopeial Convention. The United States Pharmacopeia 30—national formulary 25. Rockville, MD: The United States Pharmacopeial Convention, Inc.; 2007.
- United States Pharmacopeial Convention. The United States Pharmacopeia 41—national formulary 36. Rockville, MD: The United States Pharmacopeial Convention, Inc.; 2018.
- United States Pharmacopeial Convention. The United States Pharmacopeia 42—national formulary 37. Rockville, MD: The United States Pharmacopeial Convention, Inc.; 2019.
- US Food and Drug Administration, Center for Drug Evaluation and Research (CDER). SUPAC-MR: modified release solid oral dosage forms scale-up and postapproval changes: chemistry, manufacturing, and controls; *in vitro* dissolution testing and *in vivo* bioequivalence documentation. Rockville, MD: US Department of Health and Human Services; 1997. p. 36.
- US Food and Drug Administration, Center for Drug Evaluation and Research (CDER). Bioavailability and bioequivalence studies submitted in NDAs or INDs — general considerations. Rockville, MD: US Department of Health and Human Services; 2014.
- US Food and Drug Administration, Center for Drug Evaluation and Research (CDER). Bioavailability studies submitted in NDAs or INDs — general considerations. Rockville, MD: US Department of Health and Human Services; 2022.
- Decreto No. 12/007, apruébanse las recomendaciones técnicas para la realización de estudios de bioequivalencia. 27.165-A, Diario Oficial de la República Oriental del Uruguay. Montevideo, Uruguay: Ministerio de Salud Pública; 2007.
- Agência Nacional de Vigilância Sanitária. The Brazilian Pharmacopeia 5ª edição: volume I. Brasília, Brazil: Agência Nacional de Vigilância Sanitária; 2010. p. 546.
- Agência Nacional de Vigilância Sanitária. The Brazilian Pharmacopeia 7ª Edição: volume I. Brasília, Brazil: Agência Nacional de Vigilância Sanitária; 2024. p. 1072.
- Decreto 32470-S, reglamento para el registro sanitario de los medicamentos que requieren demostrar Equivalencia Terapéutica. San José, Costa Rica: Ministerio de Salud de Costa Rica; 2013.
- Instituto de Salud Pública de Chile. Guía Técnica G-MOVAL 01 Guía Técnica para la presentación de modificaciones a procesos productivos validados de formas farmacéuticas sólidas post demostración de Equivalencia Terapéutica. Santiago, Chile: Departamento Agencia Nacional de Medicamentos; 2018. p. 38.
- Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (ANMAT). *Farmacopea Argentina. 7a ed, Vol. 1.* Buenos Aires, Argentina: ANMAT; 2003. p. 621.
- Resolución 1124 de 2016, por la cual se establece la Guía que contiene los criterios y requisitos para el estudio de Biodisponibilidad y Bioequivalencia de medicamentos, se define el listado de los que deben presentarlos y se establecen las condiciones de las

- Instituciones que los realicen. Bogotá D.C, Colombia: Ministerio de Salud y Protección Social; 2016.
26. Norma NOM-177-SSA1-2013, establece las pruebas y procedimientos para demostrar que un medicamento es intercambiable. Requisitos a que deben sujetarse los Terceros Autorizados que realicen las pruebas de intercambiabilidad. Requisitos para realizar los estudios de biocomparabilidad. Requisitos a que deben sujetarse los Terceros Autorizados, Centros de Investigación o Instituciones Hospitalarias que realicen las pruebas de biocomparabilidad. Acapulco, Estados Unidos Mexicanos: Secretaría de Salud; 2013.
 27. Consejo de Salubridad General. Estudios de Bioequivalencia de medicamentos sólidos orales de liberación modificada. México D.F., Mexico: El Consejo; 2018. p. 13.
 28. Health Canada. Guidance document - comparative bioavailability standards: formulations used for systemic effects. Ottawa, ON: Health Canada; 2018. p. 16.
 29. Resolución S.G N-092, por la cual se aprueban la Guía técnica para la realización de los estudios de biodisponibilidad relativa/bioequivalencia (*in vivo*) para medicamentos; y los anexos respectivos. Asunción, Paraguay: Ministerio de Salud Pública y Bienestar Social; 2020.
 30. Resolución ARCSA-de-2024-038-DASP, criterios y requisitos para demostrar bioequivalencia y biodisponibilidad en los medicamentos de uso humano. R.O.S. 620, Registro Oficial 330. Quito, Ecuador: Agencia Nacional de Regulación, Control y Vigilancia Sanitaria; 2024.
 31. De Haan P, Lerk CF. Oral controlled release dosage forms: a review. *Pharm Weekbl Sci.* 1984;6(2):57–67. doi: <http://doi.org/10.1007/BF01953956>
 32. Buckley NA, Dawson AH, Reith DA. Controlled release drugs in overdose: clinical considerations. *Drug Saf.* 1995;12(1):73–84. doi: <http://doi.org/10.2165/00002018-199512010-00006>
 33. Patel V, Patel V. Pulsatile drug delivery system: a review. *Int J Pharm Sci Res.* 2015;6(9):3676–88.
 34. Trenfield SJ, Basit AW. Modified drug release: current strategies and novel technologies for oral drug delivery. In: Martins JP, Santos HA, editors. *Nanotechnology for oral drug delivery.* London, UK: Academic Press; 2020. p. 177.
 35. Ducharme M, Shargel L. Modified-release drug products and drug devices. In: Weitz M, Boyle P, editors. *Shargel and Yu's applied biopharmaceutics & pharmacokinetics.* 8th ed. New York, NY: McGraw Hill; 2022.
 36. U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Guidance for industry: orally disintegrating tablets. Silver Spring, MD: US Department of Health and Human Services; 2008. p. 3.
 37. Soares KCC, Chiann C, Storpirtis S. Assessment of the impact of partial area under the curve in a bioavailability/bioequivalence study on generic prolonged-release formulations. *Eur J Pharm Sci.* 2022;171:106127. doi: <http://doi.org/10.1016/j.ejps.2022.106127>
 38. Kir F, Al-Sulaiti FK, Sahin S. Evaluation of *in vitro* dissolution profiles of modified-release metoprolol succinate tablets crushed using mortar and pestle technique. *Eur J Pharm Sci.* 2024;194:106694. doi:<http://doi.org/10.1016/j.ejps.2024.106694>
 39. Krishnaraj K, Chandrasekar MJN, Nanjan MJ, Muralidharan S, Manikandan D. Development of sustained release antipsychotic tablets using novel polysaccharide isolated from *Delonix regia* seeds and its pharmacokinetic studies. *Saudi Pharm J.* 2012;20(3):239–48. doi: <http://doi.org/10.1016/j.jsps.2011.12.003>.
 40. You C, Liang X, Sun J, Sun L, Wang Y, Fan T, *et al.* Blends of hydrophobic and swelling agents in the swelling layer in the preparation of delayed-release pellets of a hydrophilic drug with low MW: physicochemical characterizations and *in-vivo* evaluations. *Asian J Pharm Sci.* 2014;9(4):199–207.
 41. Vattanagijyong Y, Kulvanich P, Chatchawalsaisin J. Fabrication of delayed release hard capsule shells from zein/methacrylic acid copolymer blends. *Eur J Pharm Sci.* 2022;171:106124.
 42. Nezhad Mohseni M, Najafpour Darzi G, Ramezani R, Jahani A. A developed composite hard-gelatin capsules: delayed-release enteric properties. *Heliyon.* 2022;8(12):e12265.
 43. Dhiman N, Awasthi R, Jindal S, Khatri S, Dua K. Development of bilayer tablets with modified release of selected incompatible drugs. *Polim Med.* 2016;46(1):5–15.
 44. Vlachou M, Geraniou E, Siamidi A. Modified release of furosemide from Eudragits® and poly(ethylene oxide)-based matrices and dry-coated tablets. *Acta Pharm.* 2020;70(1):49–61.
 45. Vo AQ, Kutz G, He H, Narala S, Bandari S, Repka MA. Continuous manufacturing of ketoprofen delayed release pellets using melt extrusion technology: application of QbD design space, inline near infrared, and inline pellet size analysis. *J Pharm Sci.* 2020;109(12):3598–607.
 46. Jacobsen NMY, Caglayan I, Caglayan A, Bar-Shalom D, Müllertz A. Achieving delayed release of freeze-dried probiotic strains by extrusion, spheronization and fluid bed coating - evaluated using a three-step *in vitro* model. *Int J Pharm.* 2020;591:120022.
 47. Alqahtani A, Mohammed A, Fatima F, Ahmed M. Fused deposition modelling 3D-printed gastro-retentive floating device for propranolol HCl tablets. *Polym (Basel).* 2023;15(17):3554. doi: <http://doi.org/10.3390/polym15173554>.
 48. Alhamhoom Y, Ravi G, Osmani RAM, Hani U, Prakash GM. Formulation, characterization, and evaluation of Eudragit-coated saxagliptin nanoparticles using 3 factorial design modules. *Molecules.* 2022;27(21):7510.
 49. Guittet C, Roussel-Maupetit C, Manso-Silván MA, Guillaumin F, Vandenhende F, Granier LA. Innovative prolonged-release oral alkalising formulation allowing sustained urine pH increase with twice daily administration: randomised trial in healthy adults. *Sci Rep.* 2020;10(1):13960. doi: <http://doi.org/10.1038/s41598-020-70549-2>.
 50. Aamir MN, Ahmad M. Production and stability evaluation of modified-release microparticles for the delivery of drug combinations. *AAPS PharmSciTech.* 2010;11(1):351–5. doi: <http://doi.org/10.1208/s12249-010-9392-1>.
 51. Ojsteršek T, Hudovornik G, Vrečer F. Comparative study of selected excipients' influence on carvedilol release from hypromellose matrix tablets. *Pharmaceutics.* 2023;15(5):1525. doi: <http://doi.org/10.3390/pharmaceutics15051525>.
 52. Poo J, Aguilar J, Bernal R, Alonso R, Gasca F, Hernández L, *et al.* Prolonged release pifrenidone pharmacokinetics is modified in cirrhosis GENESIS study. *Biomed Pharmacother Biomedecine Pharmacother.* 2023;168:115712. doi: <http://doi.org/10.1016/j.biopha.2023.115712>.
 53. Xu H, Liu L, Li X, Ma J, Liu R, Wang S. Extended tacrolimus release via the combination of lipid-based solid dispersion and HPMC hydrogel matrix tablets. *Asian J Pharm Sci.* 2019;14(4):445–54. doi: <http://doi.org/10.1016/j.ajps.2018.08.001>.
 54. Đuranović M, Obeid S, Madžarević M, Cvijić S, Ibrić S. Paracetamol extended release FDM 3D printlets: evaluation of formulation variables on printability and drug release. *Int J Pharmaceutics.* 2021;592:120053. doi: <http://doi.org/10.1016/j.ijpharm.2020.120053>.
 55. Zhang Y, Zhu W, Zhang H, Han J, Zhang L, Lin Q, *et al.* Carboxymethyl chitosan/phospholipid bilayer-capped mesoporous carbon nanoparticles with pH-responsive and prolonged release properties for oral delivery of the antitumor drug, Docetaxel. *Int J Pharm.* 2017;532(1):384–92. doi: <http://doi.org/10.1016/j.ijpharm.2017.09.023>.
 56. Iftime MM, Mittelu Tartau L, Marin L. New formulations based on salicyl-imine-chitosan hydrogels for prolonged drug release. *Int J Biol Macromolecules.* 2020;160:398–408. doi: <http://doi.org/10.1016/j.ijbiomac.2020.05.207>
 57. Bani-Jaber A, Al-Aani L, Alkhatib H, Al-Khalidi B. Prolonged intragastric drug delivery mediated by Eudragit® E-Carrageenan

- polyelectrolyte matrix tablets. *AAPS PharmSciTech.* 2011;12:354–61. doi: <http://doi.org/10.1208/s12249-011-9595-0>.
58. Rasul A, Maheen S, Khan HU, Rasool M, Shah S, Abbas G, *et al.* Formulation, optimization, in vitro and in vivo evaluation of saxagliptin-loaded lipospheres for an improved pharmacokinetic behavior. *Biomed Res Int.* 2021;2021:3849093. doi: <http://doi.org/10.1155/2021/3849093>.
59. Kim J, Cha K, Kang S, Won D, Jang S, Son M, *et al.* In vivo gastric residence and gastroprotective effect of floating gastroretentive tablet of DA-9601, an extract of *Artemisia asiatica*, in beagle dogs. *Drug Des Devel Ther.* 2016;10:1917–25. doi: <http://doi.org/10.2147/DDDT.S102918>.
60. Ochiuz L, Grigoras C, Popa M, Stoleriu I, Munteanu C, Timofte D, *et al.* Alendronate-loaded modified drug delivery lipid particles intended for improved oral and topical administration. *Molecules.* 2016;21(7):858. doi: <http://doi.org/10.3390/molecules21070858>.
61. Rahat I, Imam SS, Rizwanullah M, Alshehri S, Asif M, Kala C, *et al.* Thymoquinone-entrapped chitosan-modified nanoparticles: formulation optimization to preclinical bioavailability assessments. *Drug Deliv.* 2021;28(1):973–84.
62. Yang Q, Yang J, Sun S, Zhao J, Liang S, Feng Y, *et al.* Rhodojaponin III-loaded chitosan derivatives-modified solid lipid nanoparticles for multimodal antinociceptive effects in vivo. *Int J Nanomed.* 2022;17:3633–53. doi: <http://doi.org/10.2147/IJN.S362443>.
63. Gathirwa JW, Omwoyo W, Ogutu B, Oloo F, Swai H, Kalombo L, *et al.* Preparation, characterization, and optimization of primaquine-loaded solid lipid nanoparticles. *Int J Nanomed.* 2014;9:3865–74. doi: <http://doi.org/10.2147/IJN.S62630>.
64. Muheem A, Wasim M, Aldosari E, Baboota S, Ali J. Fabrication of TPGS decorated etravirine loaded lipidic nanocarriers as a neoteric oral bioavailability enhancer for lymphatic targeting. *Discov Nano.* 2024;19(1):5. doi: <http://doi.org/10.1186/s11671-023-03954-x>.
65. Ünal S, Doğan O, Aktaş Y. Orally administered docetaxel-loaded chitosan-decorated cationic PLGA nanoparticles for intestinal tumors: formulation, comprehensive in vitro characterization, and release kinetics. *Beilstein J Nanotechnol.* 2022;13:1393–407. doi: <http://doi.org/10.3762/bjnano.13.115>.
66. Lee H, Bang JB, Na YG, Lee JY, Cho CW, Baek JS, *et al.* Development and evaluation of tannic acid-coated nanosuspension for enhancing oral bioavailability of curcumin. *Pharmaceutics.* 2021;13(9):1460.
67. Hasan AA, Madkor H, Wageh S. Formulation and evaluation of metformin hydrochloride-loaded niosomes as controlled release drug delivery system. *Drug Deliv.* 2013;20(3-4):120–6. doi: <http://doi.org/10.3109/10717544.2013.779332>.
68. Samy W, Elnoby A, El-Gowelli HM, Elgindy N. Hybrid polymeric matrices for oral modified release of desvenlafaxine succinate tablets. *Saudi Pharm J.* 2017;25(5):676–87. doi: <http://doi.org/10.1016/j.jsps.2016.10.005>.
69. Lee J, Lee CH, Lee JG, Jeon SY, Choi MK, Song IS. Enhancing dissolution and oral bioavailability of ursodeoxycholic acid with a spray-dried pH-modified extended release formulation. *Pharmaceutics.* 2022;14(5):1037. doi: <http://doi.org/10.3390/pharmaceutics14051037>.
70. Arafat M, Sarfraz M, Bostanudin M, Esmaeil A, Salam A, AbuRuz S. In vitro and in vivo evaluation of oral controlled release formulation of BCS class I drug using polymer matrix system. *Pharmaceutics (Basel).* 2021;14(9):929. doi: <http://doi.org/10.3390/ph14090929>.
71. El Nabarawi M, Teaima M, Abd El-monem R, El Nabarawy N, Gaber D. Formulation, release characteristics, and bioavailability study of gastroretentive floating matrix tablet and floating raft system of mebeverine HCl. *Drug Des Devel Ther.* 2017;11:1081–93. doi: <http://doi.org/10.2147/DDDT.S131936>.
72. Barboza F, Machado W, Olchanheski L, De Paula J, Zawadzki S, Fernandes D, *et al.* PCL/PHBV microparticles as innovative carriers for oral controlled release of manidipine dihydrochloride. *ScientificWorldJournal.* 2014;2014:268107. doi: <http://doi.org/10.1155/2014/268107>.
73. Gao Z, Ngo C, Ye W, Rodriguez JD, Keire D, Sun D, *et al.* Effects of dissolution medium pH and simulated gastrointestinal contraction on drug release from nifedipine extended-release tablets. *J Pharm Sci.* 2019;108(3):1189–94. doi: <http://doi.org/10.1016/j.xphs.2018.10.014>.
74. Sandomierski M, Chojnacka M, Długosz M, Pokora M, Zwolińska J, Majchrzycki Ł, *et al.* Mesoporous silica modified with polydopamine and zinc ions as a potential carrier in the controlled release of mercaptopurine. *Mater (Basel).* 2023;16(12):4358. doi: <https://doi.org/10.3390/ma16124358>.
75. Hu X, Zhang J, Deng L, Hu H, Hu J, Zheng G. Galactose-modified pH-sensitive niosomes for controlled release and hepatocellular carcinoma target delivery of tanshinone IIA. *AAPS PharmSciTech.* 2021;22(3):96. doi: <https://doi.org/10.1208/s12249-021-01973-4>.
76. Vlachou M, Siamidi A, Anagnostopoulou D, Christodoulou E, Bikiaris N. Modified release of the pineal hormone melatonin from matrix tablets containing poly(L-lactic acid) and its PLA-co-PEAd and PLA-co-PBAd copolymers. *Polym (Basel).* 2022;14(8):1504. doi: <https://doi.org/10.3390/polym14081504>.
77. Szkutnik-Fiedler D, Balcerkiewicz M, Sawicki W, Grabowski T, Grześkowiak E, Mazgalski J, *et al.* In vitro-in vivo evaluation of a new oral dosage form of tramadol hydrochloride--controlled-release capsules filled with coated pellets. *Acta Pol Pharm.* 2014;71(3):469–75.
78. Emeje M, John-Africa L, Isimi Y, Kunle O, Ofoefule S. Eudraginated polymer blends: a potential oral controlled drug delivery system for theophylline. *Acta Pharm.* 2012;62(1):71–82. doi: <https://doi.org/10.2478/v10007-012-0001-6>.
79. Yuan Z, Gu X. Preparation, characterization, and in vivo study of rhein-loaded poly(lactic-co-glycolic acid) nanoparticles for oral delivery. *Drug Des Devel Ther.* 2015;9:2301–9. doi: <https://doi.org/10.2147/DDDT.S81320>.
80. Mumuni MA, Kenechukwu FC, Ernest OC, Oluseun AM, Abdulmumin B, Youngson DC, *et al.* Surface-modified mucoadhesive microparticles as a controlled release system for oral delivery of insulin. *Heliyon.* 2019;5(9):2366. doi: <https://doi.org/10.1016/j.heliyon.2019.e02366>.
81. Tayel SA, El-Nabarawi MA, Tadros MI, Abd-Elsalam WH. Duodenum-triggered delivery of pravastatin sodium: iI. Design, appraisal and pharmacokinetic assessments of enteric surface-decorated nanocubosomal dispersions. *Drug Deliv.* 2016;23(9):3266–78. doi: <https://doi.org/10.3109/10717544.2016.1172367>.
82. Goyanes A, Buanz A, Hatton G, Gaisford S, Basit A. 3D printing of modified-release aminosaliclylate (4-ASA and 5-ASA) tablets. *Eur J Pharm Biopharm.* 2015;89:157–62. doi: <https://doi.org/10.1016/j.ejpb.2014.12.003>.
83. Hameed HA, Khan S, Shahid M, Ullah R, Bari A, Ali SS, *et al.* Engineering of naproxen loaded polymer hybrid enteric microspheres for modified release tablets: development, characterization, in silico modelling and in vivo evaluation. *Drug Design Develop Therapy.* 2020;14:27–41. doi: <https://doi.org/10.2147/DDDT.S232111>.
84. Chang HHR, Chen K, Lugtu-Pe JA, Al-Mousawi N, Zhang X, Bar-Shalom D, *et al.* Design and optimization of a nanoparticulate pore former as a multifunctional coating excipient for pH transition-independent controlled release of weakly basic drugs for oral drug delivery. *Pharmaceutics.* 2023;15(2):547. doi: <https://doi.org/10.3390/pharmaceutics15020547>.
85. Waglewska E, Pucek-Kaczmarek A, Bazylińska U. Self-assembled bilosomes with stimuli-responsive properties as bioinspired dual-tunable nanoplatfor for pH/temperature-triggered release of hybrid cargo. *Colloids Surf B Biointerfaces.* 2022;215:112524. doi: <http://doi.org/10.1016/j.colsurfb.2022.112524>.
86. Creteanu A, Lisa G, Vasile C, Popescu MC, Pamfil D, Lungu CN, *et al.* New hydrophilic matrix tablets for the controlled release of chlorzoxazone. *Int J Mol Sci.* 2024;25(10):5137. doi: <http://doi.org/10.3390/ijms25105137>.
87. Zhang Y, Wang L, Wang ZD, Zhou Q, Zhou X, Zhou T, *et al.* Surface-anchored microbial enzyme-responsive solid lipid nanoparticles

- enabling colonic budesonide release for ulcerative colitis treatment. *J Nanobiotechnol.* 2023;21(1):145. doi: <http://doi.org/10.1186/s12951-023-01889-0>.
88. Awad A, Fina F, Trenfield SJ, Patel P, Goyanes A, Gaisford S, *et al.* 3D printed pellets (miniprintlets): a novel, multi-drug, controlled release platform technology. *Pharmaceutics.* 2019;11(4):148.
 89. Arafat M, Sarfraz M, AbuRuz S. Development and in vitro evaluation of controlled release Viagra® containing poloxamer-188 using Gastroplus™ PBPK modeling software for in vivo predictions and pharmacokinetic assessments. *Pharmaceutics (Basel).* 2021;14(5):479.
 90. Kim J, Lee S, Park C, Rhee Y, Kim D, Park J, *et al.* Design and in vivo evaluation of oxycodone once-a-day controlled-release tablets. *Drug Des Devel Ther.* 2015;9:695–706. doi: <http://doi.org/10.3390/pharmaceutics11040148>.
 91. Patel N, Lalwani D, Gollmer S, Injeti E, Sari Y, Nesamony J. Development and evaluation of a calcium alginate based oral ceftriaxone sodium formulation. *Prog Biomater.* 2016;5(1-4):117–33.
 92. Huanbutta K, Sittikijyothin W. Use of seed gums from *Tamarindus indica* and *Cassia fistula* as controlled-release agents. *Asian J Pharm Sci.* 2018;13(5):398–408. doi: <http://doi.org/10.1007/s40204-016-0051-9>.
 93. Piao Z, Lee K, Kim D, Lee H, Lee J, Oh K, *et al.* Comparison of release-controlling efficiency of polymeric coating materials using matrix-type casted films and diffusion-controlled coated tablets. *AAPS PharmSciTech.* 2010;11(2):630–6. doi: <http://doi.org/10.1208/s12249-010-9377-0>.
 94. Jeganathan B, Prakya V. Interpolyelectrolyte complexes of Eudragit® EPO with hypromellose acetate succinate and Eudragit® EPO with hypromellose phthalate as potential carriers for oral controlled drug delivery. *AAPS PharmSciTech.* 2015;16(4):878–88. doi: <http://doi.org/10.1208/s12249-014-0252-2>.
 95. Rasool F, Ahmad M, Murtaza G, Khan HMS, Khan SA. Eudragit FS based colonic microparticles of metoprolol tartrate. *Acta Pol Pharm.* 2012;69(2):347–53.
 96. Liu Z, Zhou D, Liao L. PH/redox/lysozyme-sensitive hybrid nanocarriers with transformable size for multistage drug delivery. *Front Bioeng Biotechnol.* 2022;10:882308. doi: <http://doi.org/10.3389/fbioe.2022.882308>
 97. Reis S, Neves, Lúcio, Martins, Lima. Novel resveratrol nanodelivery systems based on lipid nanoparticles to enhance its oral bioavailability. *Int J Nanomed.* 2013;8:177–87. doi: <http://doi.org/10.2147/IJN.S37840>
 98. Ullah F, Iqbal Z, Khan A, Khan S, Ahmad L, Alotaibi A, *et al.* Formulation development and characterization of pH responsive polymeric nanopharmaceuticals for targeted delivery of anticancer drug (methotrexate). *Front Pharmacol.* 2022;13:911771. doi: <http://doi.org/10.3389/fphar.2022.911771>.
 99. Khan S, Ahmad M, Murtaza G, Aamir M, Akhtar N, Kousar R. Formulation of two-drug controlled release non-biodegradable microparticles for potential treatment of muscle pain and spasm and their simultaneous spectrophotometric estimation. *Acta Pol Pharm.* 2010;67(3):299–306.
 100. Liu H, Li Y, Zhang X, Shi M, Li D, Wang Y. Chitosan-coated solid lipid nano-encapsulation improves the therapeutic anti-airway inflammation effect of berberine against COPD in cigarette smoke-exposed rats. *Can Respir J.* 2022;2022:8509396. doi: <http://doi.org/10.1155/2022/8509396>.
 101. Tidau M, Finke JH. Modified release kinetics in dual filament 3D printed individualized oral dosage forms. *Eur J Pharm Sci.* 2022;175:106221. doi: <http://doi.org/10.1016/j.ejps.2022.106221>.
 102. Mubeen I, Zaman M, Farooq M, Mehmood A, Azeez F, Rehman W, *et al.* Formulation of modified-release bilayer tablets of atorvastatin and ezetimibe: an *in-vitro* and *in-vivo* analysis. *Polym (Basel).* 2022;14(18):3770. doi: <http://doi.org/10.3390/polym14183770>.
 103. Gaikwad SS, Kshirsagar SJ. Application of tablet in tablet technique to design and characterize immediate and modified release tablets of timolol maleate. *Heliyon.* 2024;10(3):e25820. doi: <http://doi.org/10.1016/j.heliyon.2024.e25820>.
 104. Cha KH, Tran TH, Kim MS, Kim JS, Park HJ, Park J, *et al.* PH-independent sustained release matrix tablet containing doxazosin mesylate: effect of citric acid. *Arch Pharm Res.* 2010;33(12):2003–9. doi: <http://doi.org/10.1007/s12272-010-1216-z>.
 105. Zhang C, Zhao Q, Wan L, Wang T, Sun J, Gao Y, *et al.* Poly(dimethyl diallyl ammonium) coated CMK-5 for sustained oral drug release. *Int J Pharm.* 2014;461(1-2):171–80. doi: <http://doi.org/10.1016/j.ijpharm.2013.11.050>.
 106. Hu L, Sun H, Zhao Q, Han N, Bai L, Wang Y, *et al.* Multilayer encapsulated mesoporous silica nanospheres as an oral sustained drug delivery system for the poorly water-soluble drug felodipine. *Mater Sci Eng C.* 2015;47:313–24. doi: <http://doi.org/10.1016/j.msec.2014.10.067>.
 107. Zhang Y, Zhang H, Che E, Zhang L, Han J, Yang Y, *et al.* Development of novel mesoporous nanomatrix-supported lipid bilayers for oral sustained delivery of the water-insoluble drug, lovastatin. *Colloids Surf B Biointerfaces.* 2015;128:77–85. doi: <http://doi.org/10.1016/j.colsurfb.2015.02.021>.
 108. Gao Y, Jin X, Sun Y, Xu FF, Zhang M. Production and investigation of sustained berberine pellet drug release system. *Adv Powder Technol.* 2018;29(3):682–91. doi: <https://doi.org/10.1016/j.apm.2017.12.011>.
 109. Dong L, Yang F, Zhu Z, Yang Y, Zhang X, Ye M, *et al.* Preparation, characterization and pharmacokinetics evaluation of the compound capsules of ibuprofen enteric-coated sustained-release pellets and codeine phosphate immediate-release pellets. *AAPS PharmSciTech.* 2018;19(7):3057–66. doi: <https://doi.org/10.1208/s12249-018-1119-8>.
 110. Tian MP, Song RX, Wang T, Sun MJ, Liu Y, Chen XG. Inducing sustained release and improving oral bioavailability of curcumin via chitosan derivatives-coated liposomes. *Int J Biol Macromol.* 2018;120:702–10. doi: <https://doi.org/10.1016/j.ijbiomac.2018.08.146>.
 111. Ashraf M, Hussain M, Bashir S, Haseeb M, Hussain Z. Quince seed hydrogel (glucuronoxylan): evaluation of stimuli responsive sustained release oral drug delivery system and biomedical properties. *J Drug Deliv Sci Technol.* 2018;45:455–65. doi: <https://doi.org/10.1016/j.jddst.2018.04.008>.
 112. Četković Z, Cvijić S, Vasiljević D. Formulation and characterization of novel lipid-based drug delivery systems containing polymethacrylate polymers as solid carriers for sustained release of simvastatin. *J Drug Deliv Sci Technol.* 2019;53:101222. doi: <https://doi.org/10.1016/j.jddst.2019.101222>.
 113. Ailincăi D, Gavril G, Marin L. Poly(vinyl alcohol)-boric acid: a promising tool for the development of sustained release drug delivery systems. *Mater Sci Eng C.* 2020;107:110316. doi: <https://doi.org/10.1016/j.msec.2019.110316>.
 114. Khairnar G, Mokale V, Mujumdar A, Naik J. Development of nanoparticulate sustained release oral drug delivery system for the antihyperglycemic with antihypertensive drug. *Mater Technol.* 2019;34(14):880–8. doi: <https://doi.org/10.1080/10667857.2019.1639019>.
 115. Sharma S, Sarkar G, Srestha B, Chattopadhyay D, Bhowmik M. *In-situ* fast gelling formulation for oral sustained drug delivery of paracetamol to dysphagic patients. *Int J Biol Macromol.* 2019;134:864–8. doi: <https://doi.org/10.1016/j.ijbiomac.2019.05.092>.
 116. Si S, Li H, Han X. Sustained release olmesartan medoxomil loaded PLGA nanoparticles with improved oral bioavailability to treat hypertension. *J Drug Deliv Sci Technol.* 2020;55:101422. doi: <https://doi.org/10.1016/j.jddst.2019.101422>.
 117. Bagde A, Patel N, Patel K, Nottingham E, Singh M. Sustained release dosage form of nescapine HCl using hot melt extrusion (HME) technique: formulation and pharmacokinetics. *Drug Deliv Transl Res.* 2021;11(3):1156–65. doi: <https://doi.org/10.1007/s13346-020-00838-w>.
 118. Hou J, Yang J, Zheng X, Wang M, Liu Y, Yu DG. A nanofiber-based drug depot with high drug loading for sustained release.

- Int J Pharm. 2020;583:119397. doi: <https://doi.org/10.1016/j.ijpharm.2020.119397>.
119. Xiao L, Poudel AJ, Huang L, Wang Y, Abdalla AME, Yang G. Nanocellulose hyperfine network achieves sustained release of berberine hydrochloride solubilized with β -cyclodextrin for potential anti-infection oral administration. *Int J Biol Macromol.* 2020;153:633–40. doi: <https://doi.org/10.1016/j.ijbiomac.2020.03.030>.
120. Liu H, Zhang B, Chen Y, Cui Z, Hu L. Novel microporous resin-based polymer device for sustained glipizide release: production, characterization and pharmacokinetic study. *Biomed Pharmacother.* 2022;155:113772. doi: <https://doi.org/10.1016/j.biopha.2022.113772>.
121. Hashem HM, Motawea A, Kamel AH, Bary EMA, Hassan SSM. Fabrication and characterization of electrospun nanofibers using biocompatible polymers for the sustained release of venlafaxine. *Sci Rep.* 2022;12(1):18037. doi: <https://doi.org/10.1038/s41598-022-22878-7>.
122. Shin S, Kim TH, Jeong SW, Chung SE, Lee DY, Kim DH, *et al.* Development of a gastroretentive delivery system for acyclovir by 3D printing technology and its *in vivo* pharmacokinetic evaluation in Beagle dogs. *PLoS One.* 2019;14(5):216875. doi: <https://doi.org/10.1371/journal.pone.0216875>.
123. Awasthi R, Kulkarni GT, Ramana MV, De Jesus Andreoli Pinto T, Kikuchi IS, Molim Ghisleni DD, *et al.* Dual crosslinked pectin-alginate network as sustained release hydrophilic matrix for repaglinide. *Int J Biol Macromol.* 2017;97:721–32. doi: <https://doi.org/10.1016/j.ijbiomac.2017.01.050>.
124. Kamguyan K, Kjeldsen RB, Moghaddam SZ, Nielsen MR, Thormann E, Zór K, *et al.* Bioadhesive tannic-acid-functionalized zein coating achieves engineered colonic delivery of IBD therapeutics via reservoir microdevices. *Pharmaceutics.* 2022;14(11):2536. doi: <https://doi.org/10.3390/pharmaceutics14112536>.
125. Abdelkader H, Abdel-Alem J, Mousa H, Elgendy M, Al Fatease A, Abou-Taleb H. Captopril polyvinyl alcohol/sodium alginate/gelatin-based oral dispersible films (ODFs) with modified release and advanced oral bioavailability for the treatment of pediatric hypertension. *Pharmaceutics (Basel).* 2023;16(9):1323. doi: <https://doi.org/10.3390/ph16091323>.
126. Husain T, Shoaib MH, Ahmed FR, Yousuf RI, Farooqi S, Siddiqui F, *et al.* Investigating halloysite nanotubes as a potential platform for oral modified delivery of different BCS class drugs: characterization, optimization, and evaluation of drug release kinetics. *Int J Nanomed.* 2021;16:1725–41. doi: <https://doi.org/10.2147/IJN.S299261>
127. Lu CH, Huang YF, Chu IM. Design of oral sustained-release pellets by modeling and simulation approach to improve compliance for repurposing sobrerol. *Pharmaceutics.* 2022;14(1):167. doi: <https://doi.org/10.3390/pharmaceutics14010167>.
128. De Thaye E, Vervaek A, Marostica E, Remon JP, Van Bocxlaer J, Vervaeck C, *et al.* Pharmacokinetic analysis of modified-release metoprolol formulations: an interspecies comparison. *Eur J Pharm Sci.* 2017;97:135–42.
129. De Marco I. Coprecipitation of class II NSAIDs with polymers for oral delivery. *Polym (Basel).* 2023;15(4):954. doi: <https://doi.org/10.3390/polym15040954>.
130. Kim DD, Cho HJ, Park JW, Yoon IS. Surface-modified solid lipid nanoparticles for oral delivery of docetaxel: enhanced intestinal absorption and lymphatic uptake. *Int J Nanomed.* 2014;9:495–504. doi: <https://doi.org/10.2147/IJN.S56648>.
131. Li Y, Zhu C. Mechanism of hepatic targeting via oral administration of DSPE-PEG-cholic acid-modified nanoliposomes. *Int J Nanomed.* 2017;12:1673–84. doi: <https://doi.org/10.2147/IJN.S125047>.
132. Cheng Y, Wu I, Chen Y, Chu I. Thermo-sensitive mPEG-PA-PLL hydrogel for drug release of calcitonin. *Gels (Basel).* 2022;8(5):282. doi: <https://doi.org/10.3390/gels8050282>.
133. Ahmed O, Hosny K, Al-Sawahli M, Fahmy U. Optimization of caseinate-coated simvastatin-zein nanoparticles: improved bioavailability and modified release characteristics. *Drug Design Develop Therapy.* 2015;9:655–62. doi: <https://doi.org/10.2147/DDDT.S76194>.
134. Tian C, Asghar S, Wu Y, Chen Z, Jin X, Yin L, *et al.* Improving intestinal absorption and oral bioavailability of curcumin via taurocholic acid-modified nanostructured lipid carriers. *Int J Nanomed.* 2017;12:7897–911. doi: <https://doi.org/10.2147/IJN.S145988>.
135. Xu L, Yang Q, Qiang W, Li H, Zhong W, Pan S, *et al.* Hydrophilic excipient-independent drug release from SLA-printed pellets. *Pharmaceutics.* 2021;13(10):1717. doi: <https://doi.org/10.3390/pharmaceutics13101717>.
136. Siamidi A, Dedeloudi A, Vlachou M. Probing the release of bupropion and naltrexone hydrochloride salts from biopolymeric matrices of diverse chemical structures. *Polym (Basel).* 2021;13(9):1456. doi: <https://doi.org/10.3390/polym13091456>.
137. Patel B, Parikh R, Aboti P. Development of oral sustained release rifampicin loaded chitosan nanoparticles by design of experiment. *J Drug Deliv.* 2013;2013:370938. doi: <https://doi.org/10.1155/2013/370938>.
138. Tan F, Li H, Zhang K, Xu L, Zhang D, Han Y, *et al.* Sodium alginate/chitosan-coated liposomes for oral delivery of hydroxy- α -sanshool: *in vitro* and *in vivo* evaluation. *Pharmaceutics.* 2023;15(7):2010. doi: <https://doi.org/10.3390/pharmaceutics15072010>.
139. Peng W, Jiang XY, Zhu Y, Omari-Siaw E, Deng WW, Yu JN, *et al.* Oral delivery of capsaicin using MPEG-PCL nanoparticles. *Acta Pharmacol Sin.* 2015;36(1):139–48. doi: <https://doi.org/10.1038/aps.2014.113>.
140. Guo Z, Afza R, Moneeb Khan M, Khan SU, Khan MW, Ali Z, *et al.* Investigation of the treatment potential of raloxifene-loaded polymeric nanoparticles in osteoporosis: *in-vitro* and *in-vivo* analyses. *Heliyon.* 2023;9(9):e20107. doi: <https://doi.org/10.1016/j.heliyon.2023.e20107>.
141. Racles C, Zaltariov M, Peptanariu D, Vasiliu T, Cazacu M. Functionalized mesoporous silica as doxorubicin carriers and cytotoxicity boosters. *Nanomaterials (Basel).* 2022;12(11):1823. doi: <https://doi.org/10.3390/nano12111823>.
142. Xi Y, Wang W, Ma L, Xu N, Shi C, Xu G, *et al.* Alendronate modified mPEG-PLGA nano-micelle drug delivery system loaded with astragaloside has anti-osteoporotic effect in rats. *Drug Deliv.* 2022;29(1):2386–402. doi: <https://doi.org/10.1080/10717544.2022.2086942>.
143. Wiwattanapatapee R, Klabklay K, Raksajit N, Siripruekpong W, Leelakanok N, Petchsomrit A. The development of an *in-situ* biopolymer-based floating gel for the oral delivery of metformin hydrochloride. *Heliyon.* 2023;9(4):e14796. doi: <https://doi.org/10.1016/j.heliyon.2023.e14796>.
144. Kenechukwu FC, Isaac GT, Nnamani DO, Momoh MA, Attama AA. Enhanced circulation longevity and pharmacodynamics of metformin from surface-modified nanostructured lipid carriers based on solidified reverse micellar solutions. *Heliyon.* 2022;8(3):9100. doi: <https://doi.org/10.1016/j.heliyon.2022.e09100>.
145. Qin L, Wu H, Xu E, Zhang X, Guan J, Zhao R, *et al.* Exploring the potential of functional polymer-lipid hybrid nanoparticles for enhanced oral delivery of paclitaxel. *Asian J Pharm Sci.* 2021;16(3):387–95. doi: <https://doi.org/10.1016/j.ajps.2021.02.004>.
146. Wei L, Yang Y, Shi K, Wu J, Zhao W, Mo J. Preparation and characterization of loperamide-loaded dynasan 114 solid lipid nanoparticles for increased oral absorption in the treatment of diarrhea. *Front Pharmacol.* 2016;7:332. doi: <https://doi.org/10.3389/fphar.2016.00332>.
147. Satishbabu B, Ravi R, Sandeep V, Shrutinag R. Formulation and evaluation of floating drug delivery system of famotidine. *Indian J Pharm Sci.* 2010;72(6):738–44. doi: <https://doi.org/10.4103/0250-474X.84583>.
148. Madgulkar A, Bhalekar M, Padalkar R, Shaikh M. Optimization of carboxymethyl-xyloglucan-based tramadol matrix tablets using

- simplex centroid mixture design. *J Pharm.* 2013;2013:396468. doi: <https://doi.org/10.1155/2013/396468>.
149. Öztürk A, Yenilmez E, Özarda M. Clarithromycin-loaded poly(lactic-co-glycolic acid) (PLGA) nanoparticles for oral administration: effect of polymer molecular weight and surface modification with chitosan on formulation, nanoparticle characterization and antibacterial effects. *Polym (Basel).* 2019;11(10):1632. doi: <https://doi.org/10.3390/polym11101632>.
 150. Nayak A, Malakar J. Formulation and in vitro evaluation of hydrodynamically balanced system for theophylline delivery. *J Basic Clin Pharm.* 2011;2(3):133–7.
 151. Liang Q, Xiang H, Li X, Luo C, Ma X, Zhao W, *et al.* Development of rifapentine-loaded PLGA-based nanoparticles: in vitro characterisation and in vivo study in mice. *Int J Nanomed.* 2020;15:7491–507. doi: <https://doi.org/10.2147/IJN.S257758>.
 152. Wang X, Liu Y, Li Y, Guo M, Wang A, Feng Y, *et al.* Mannosylated-chitosan-coated andrographolide nanoliposomes for the treatment of hepatitis: in vitro and in vivo evaluations. *Pharmaceuticals (Basel).* 2023;13(2):193. doi: <https://doi.org/10.3390/membranes13020193>.
 153. Li Q, Xue F, Qu J, Liu L, Hu R, Liu C. Nano-in-micro delivery system prepared by co-axial air flow for oral delivery of conjugated linoleic acid. *Mar Drugs.* 2018;17(1):15. doi: <https://doi.org/10.3390/md17010015>.
 154. Chinaeke EE, Chime SA, Onyishi VI, Attama AA, Okore VC. Formulation development and evaluation of the anti-malaria properties of sustained release artesunate-loaded solid lipid nanoparticles based on phytolipids. *Drug Deliv.* 2015;22(5):652–65. doi: <https://doi.org/10.3109/10717544.2014.881633>.
 155. Alruwaili NK, Zafar A, Alsaidan OA, Yasir M, Mostafa EM, Alnomasy SF, *et al.* Development of surface modified bilosomes for the oral delivery of quercetin: optimization, characterization *in-vitro* antioxidant, antimicrobial, and cytotoxicity study. *Drug Deliv.* 2022;29(1):3035–50. doi: <https://doi.org/10.1080/10717544.2022.2122634>.
 156. Mohanty S, Konkimalla VB, Pal A, Sharma T, Si SC. Naringin as sustained delivery nanoparticles ameliorates the anti-inflammatory activity in a Freund's complete adjuvant-induced arthritis model. *ACS Omega.* 2021;6(43):28630–941. doi: <https://doi.org/10.1021/acsomega.1c03066>.
 157. Ma Y, He S, Ma X, Hong T, Li Z, Park K, *et al.* Silymarin-loaded nanoparticles based on stearic acid-modified Bletilla striata polysaccharide for hepatic targeting. *Molecules.* 2016;21(3):265. doi: <https://doi.org/10.3390/molecules21030265>.
 158. Ayyoubi S, Cerda JR, Fernández-García R, Knief P, Lalatsa A, Healy AM, *et al.* 3D printed spherical mini-tablets: geometry versus composition effects in controlling dissolution from personalised solid dosage forms. *Int J Pharm.* 2021;597:120336. doi: <https://doi.org/10.1016/j.ijpharm.2021.120336>.
 159. Duong TT, Isomäki A, Paaaver U, Laidmäe I, Tõnisoo A, Yen TTH, *et al.* Nanoformulation and evaluation of oral berberine-loaded liposomes. *Molecules.* 2021;26(9):2591. doi: <https://doi.org/10.3390/molecules26092591>.
 160. Jain S, Datta M. Montmorillonite-PLGA nanocomposites as an oral extended drug delivery vehicle for venlafaxine hydrochloride. *Appl Clay Sci.* 2014;99:42–7. doi: <https://doi.org/10.1016/j.clay.2014.06.006>.
 161. Kruk K, Szekalska M, Basa A, Winnicka K. The impact of hypromellose on pharmaceutical properties of alginate microparticles as novel drug carriers for posaconazole. *Int J Mol Sci.* 2023;24(13):10793.
 162. Zakaria MY, Georghiou PE, Banoub JH, Beshay BY. Inclusion of a phytomedicinal flavonoid in biocompatible surface-modified chylomicron mimic nanovesicles with improved oral bioavailability and virucidal activity: molecular modeling and pharmacodynamic studies. *Pharmaceutics.* 2022;14(5):905.
 163. Bellinger AM, Jafari M, Grant TM, Zhang S, Slater HC, Wenger EA, *et al.* Oral, ultra-long-lasting drug delivery: application toward malaria elimination goals. *Sci Transl Med.* 2016;8(365):365. doi: <https://doi.org/10.1126/scitranslmed.aag2374>.
 164. Li H, Zhang M, Xiong L, Feng W, Williams RO. Bioavailability improvement of carbamazepine via oral administration of modified-release amorphous solid dispersions in rats. *Pharmaceutics.* 2020;12(11):1023. doi: <https://doi.org/10.3390/pharmaceutics12111023>.
 165. Snyder C, Clark R, Caricofe R, Bush M, Roth M, Page S, *et al.* Pharmacokinetics of 2 novel formulations of modified-release oral testosterone alone and with finasteride in normal men with experimental hypogonadism. *J Androl.* 2010;31(6):527–35. doi: <https://doi.org/10.2164/jandrol.109.009746>.
 166. Derendorf H, Ruebsamen K, Clarke L, Schaeffler A, Kirwan JR. Pharmacokinetics of modified-release prednisone tablets in healthy subjects and patients with rheumatoid arthritis. *J Clin Pharmacol.* 2013;53(3):326–33. doi: <https://doi.org/10.1177/0091270012444315>.
 167. Vlachou M, Kikionis S, Siamidi A, Tragou K, Kapoti S, Ioannou E, *et al.* Fabrication and characterization of electrospun nanofibers for the modified release of the chronobiotic hormone melatonin. *Curr Drug Deliv.* 2019;16(1):79–85. doi: <https://doi.org/10.2174/1567201815666180914095701>.
 168. Poonia N, Kharb R, Lather V, Pandita D. Nanostructured lipid carriers: versatile oral delivery vehicle. *Future Sci OA.* 2016;15(3):FSO135. doi: <https://doi.org/10.4155/fsoa-2016-0030>.
 169. Yin J, Hou Y, Song X, Wang P, Li Y. Cholate-modified polymer-lipid hybrid nanoparticles for oral delivery of quercetin to potentiate the antileukemic effect. *Int J Nanomed.* 2019;14:4045–57. doi: <https://doi.org/10.2147/IJN.S210057>.
 170. Pereira ADSBF, De Souza Lima ML, Da Silva-junior AA, Dos Santos Silva E, De Araújo Júnior RF, Martins AA, *et al.* In vitro-in vivo availability of metformin hydrochloride-PLGA nanoparticles in diabetic rats in a periodontal disease experimental model. *Pharm Biol.* 2021;59(1):1576–84. doi: <https://doi.org/10.1080/13880209.2021.2002369>.
 171. Parvez S, Yadagiri G, Gedda MR, Singh A, Singh OP, Verma A, *et al.* Modified solid lipid nanoparticles encapsulated with Amphotericin B and Paromomycin: an effective oral combination against experimental murine visceral leishmaniasis. *Sci Rep.* 2020;10(1):12243. doi: <https://doi.org/10.1038/s41598-020-69276-5>.
 172. Ding Q, Liu W, Liu X, Ding C, Zhao Y, Dong L, *et al.* Polyvinylpyrrolidone-modified taxifolin liposomes promote liver repair by modulating autophagy to inhibit activation of the TLR4/NF- κ B signaling pathway. *Front Bioeng Biotechnol.* 2022;10:860515. doi: <https://doi.org/10.3389/fbioe.2022.860515>.
 173. Sachdeva C, Mishra N, Sharma S. Development and characterization of enteric-coated microparticles of biochanin A for their beneficial pharmacological potential in estrogen deficient-hypertension. *Drug Deliv.* 2016;23(6):2044–57. doi: <https://doi.org/10.3109/10717544.2015.1114046>.

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