



PHARMACEUTICAL FORMS WITH MODIFIED RELEASE. APPLICATIONS AND PROSPECTS



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INTRODUCTION

Modified release is an important tool in maintaining therapeutic plasma concentration for prolonged periods, reducing dosing frequency and improving patient adherence. By controlling the rate, time, and site of drug release, these systems minimize fluctuations in plasma concentration and adverse effects. Modified release technologies adapt drug exposure to physiological factors namingly circadian rhythm, gastrointestinal pH, hepatic metabolism, or renal clearance.

PURPOSE OF THE WORK

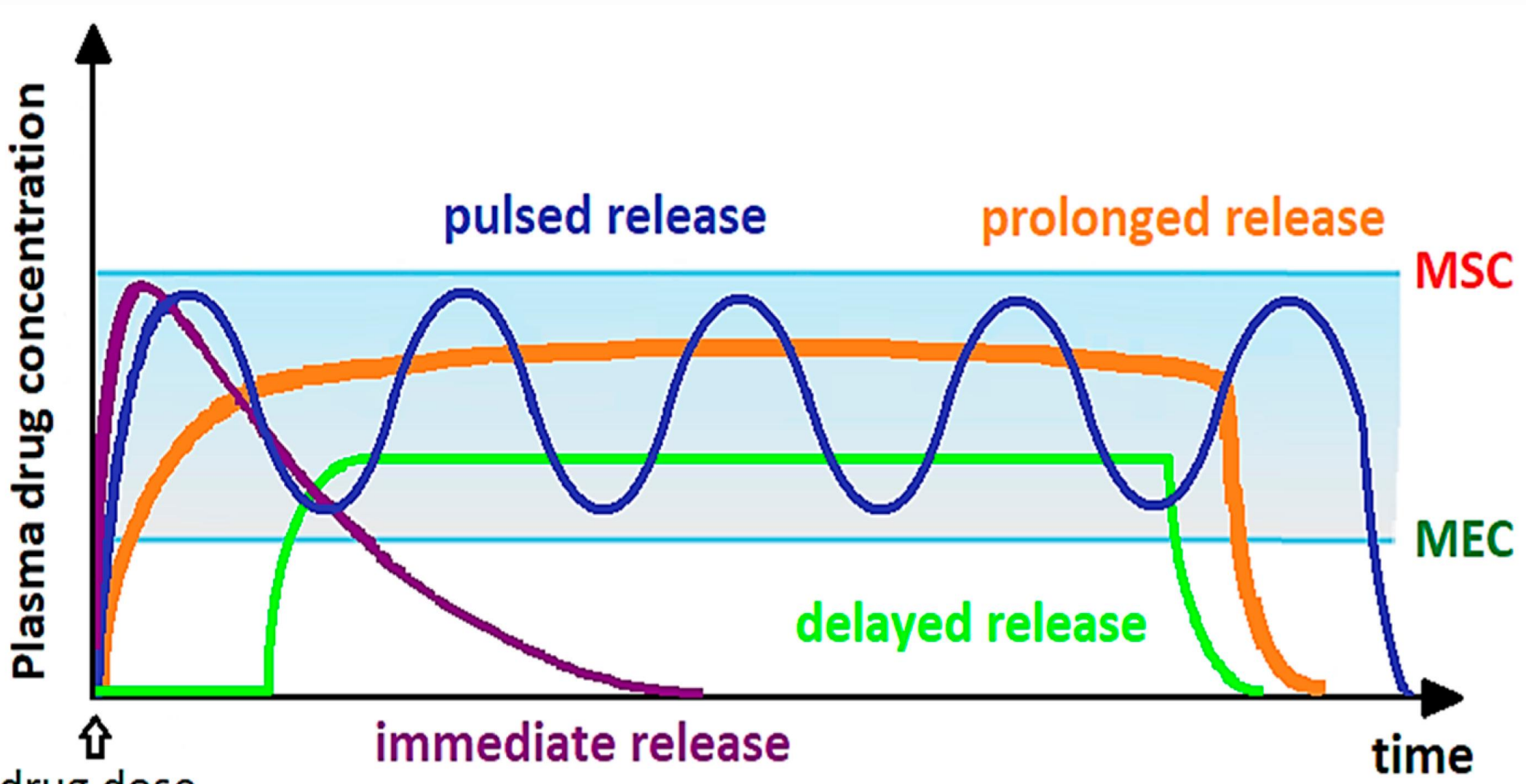
Study of the specialized literature on the modified release pharmaceutical forms, their applications and prospects.

MATERIAL AND METHODS

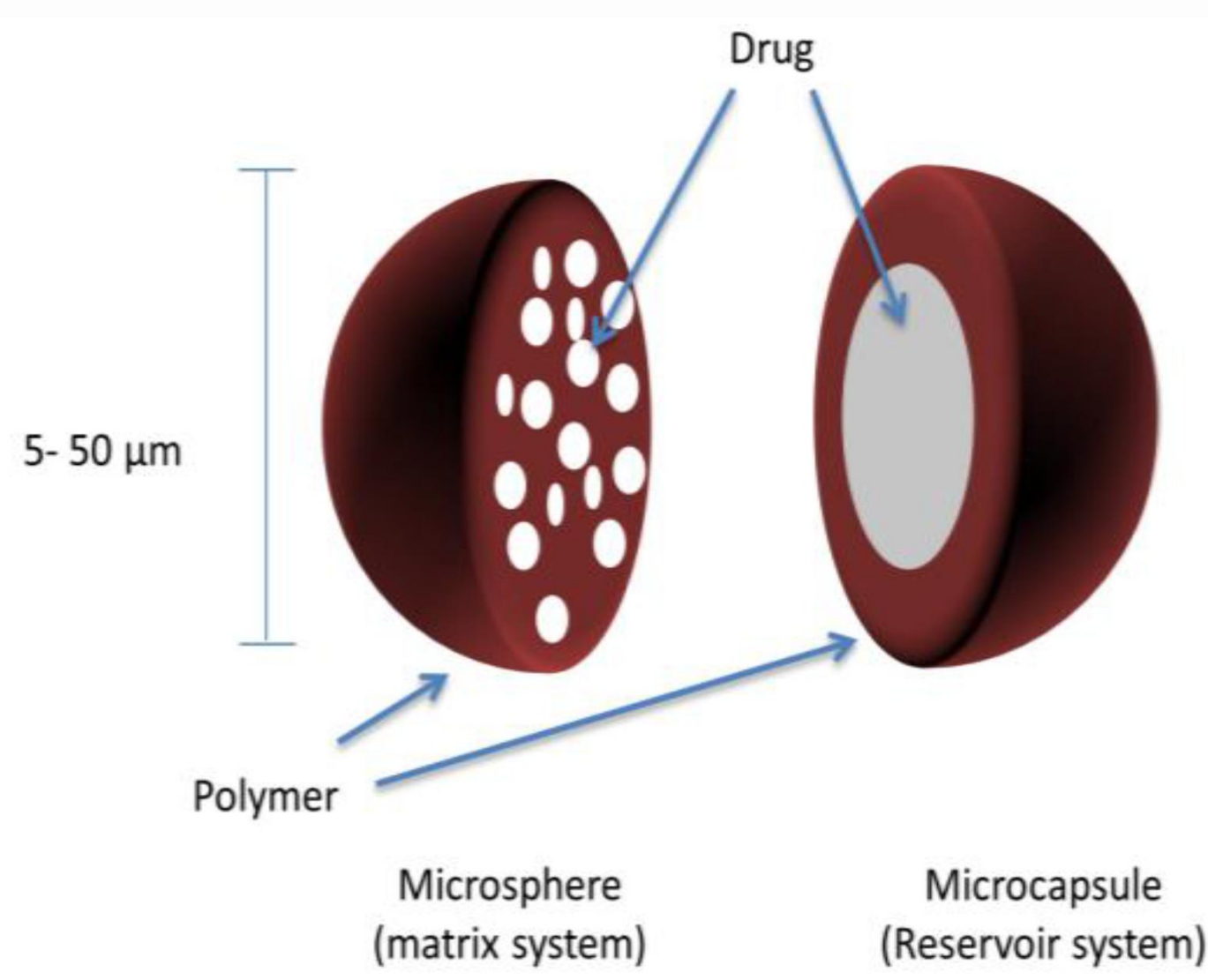
The bibliographic review in the field of pharmaceutical forms with modified release followed by the systematic research of information in Moldovan IBN and international databases: Embase and Web of Science.

KEYWORDS

Modified-release formulations, Chronopharmacology, Matrix systems, Osmotic drug delivery, Smart polymers



Graph depicting drug release
<https://doi.org/10.3390/pr8080938>



Microparticles matrix and reservoir systems
<https://doi.org/10.3390/pharmaceutics10040176>

CONCLUSIONS

Modified release pharmaceutical forms improve pharmacotherapy as they optimize pharmacokinetics, reduce adverse effects incidence, and enhance patients' adherence. The integration of chronobiology, intelligent materials and controlled release technologies represents a bright future of personalized, efficient, and safe drug administration.

RESULTS

Modified release systems are classified as extended-release, delayed-release or pulsatile (tab. 1). Matrix systems provides diffusion controlled release. It uses some hydrophilic polymers like HPMC that form a gel layer to modulate water penetration and thus also influence on the drug's diffusion. It could also use hydrophobic ones namingly ethylcellulose or stearic acid derivates that would form a water insoluble matrice.

Osmotic systems achieve zero-order kinetics through semipermeable membranes. PH-dependant coatings like cellulose acetate phthalate contribute to the protection of acid labile drugs while Eudragit® L and S (methacrylic acid copolymers) ensure a site specific intestinal release. Moreover Pulsatile or chronopharmaceutical systems synchronise drug delivery with circadian variations in disease activity such as nocturnal asthma or morning hypertension. These approches improve bioavailability and therapeutic efficiency while side effects. As of currently, reaserches focus more on smart polymers, multi-layer tablets and nano-carriers that respond to physiological stimuli such as pH, temperature and enzyme activity. These systems share the aim of enabling a greater predictability of pharmacological action and thus a more individualized therapy.

Table 1. Classification of modified release systems

Release type	Drug delivery system	Main excipients/ polymers	Technology	Examples
Extended release	Matrix systems	Hydrophilic:HPMC, Na-CMC, PEO Hydrophobic: Ethylcellulose, stearic acid derivates	Drug dispersed in polymer matrix; release by diffusion or erosion	Metformin XR, Diclofenac SR,
	Reservoir systems	Ethylcellylose, polyvinyl acetate, Eudragit® cx RL/RS	Drug core coated with rate controlling polymer film; release via diffusion through membrane	Verapamil SR, Nifedipine CR
	Osmotic systems	Semi permeable membrane: Cellulose acetate Osmotic agents: NaCl, mannitol, sucrose	Water influx creates osmotic pressure pushing drug solution through laser drilled orifice creating a zero order release	Prazosin osmotic tablets
Delayed release	pH dependant systems	Cellulose acetate phthalate, HPMCP, Eudragit® L&S	Coating remains intact in acidic pH but dissolves at intestinal pH>5.5 to create a site specific intestinal release	Omeprazole EC Erythromycin EC
Pulsatile release	Lag time systems	Eudragit® , HPMC, press-coated polymers	Drug released after predetermined lag time to match circadian rhythm or disease pattern	Propranolol chronotherapy, Diltiazem CR