Formulation characteristics of modified-release pharmaceutical dosage forms in the Republic of Serbia

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INTRODUCTION

The 11th European Pharmacopoeia defines modified-release pharmaceutical dosage forms as those that use special manufacturing techniques or substances to alter the release location or rate of the active ingredient. In the republic of Serbia, there are a total of 27 modified-release drug formulations. These formulations aim to improve compliance, reduce dosage and side effects, and enhance selectivity and efficiency.

METHODS/DESIGN

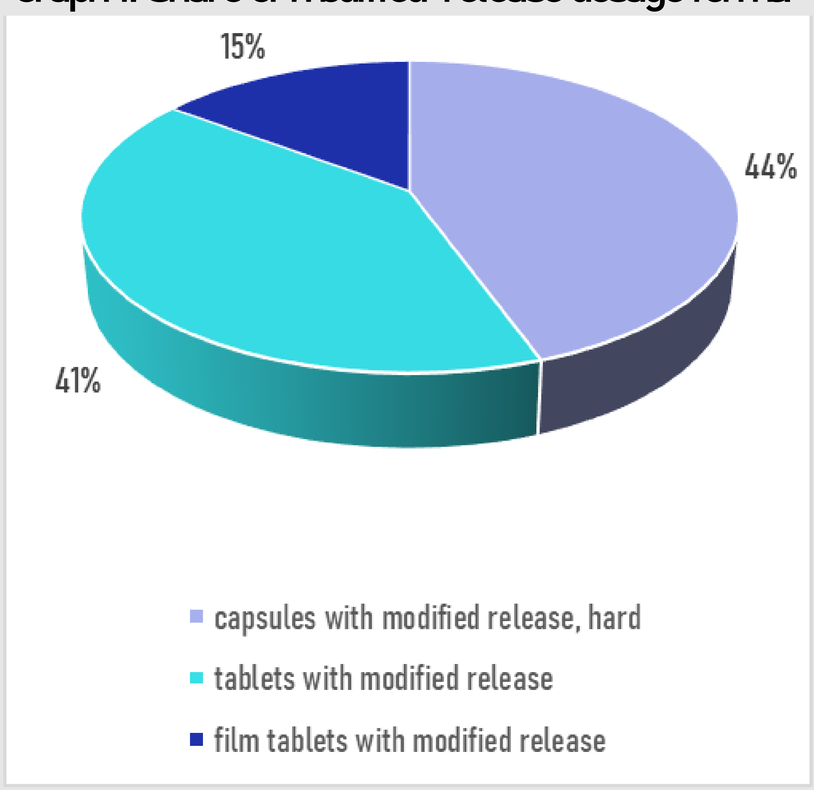
Data were collected from the official ALIMS website and the Mediately database. The methodology involved reviewing scientific literature through database searches.

RESULTS

Modified-release preparations in the Republic of Serbia can be seen in Table 1. Out of 27 modified-release drug formulations, the most common are those with tamsulosin, followed by diclofenac and gliclazide. The fewest are formulations containing mebeverine, indapamide, carbamazepine, trimetazidine, ketoprofen, and combinations of valsartan-indapamide and diclofenac-omeprazole.

The largest share (44%) are hard capsules with modified release, followed by modified-release tablets (41%), and the smallest share (15%) are film tablets with modified release (Graph 1.).

Graph 1. Share of modified-release dosage forms.



Name of the drug	INN	Dose (mg)	Form	ATC
Betamsal®	tamsulosin	0,4	capsules with modified release, hard	G04CA02
DiaclideTM MR	gliclazide	60	tablets with modified release	A10BB09
Diaprel® MR	gliclazide	60	tablets with modified release	A10BB10
Diklofenak Forte HF	diclofenac	100	tablets with modified release	M01AB05
Diprian	gliclazide	80	tablets with modified release	A10BB09
Flosin®	tamsulosin	0,4	capsules with modified release, hard	G04CA02
Fromilid® uno	clarithromycin	500	film tablets with modified release	J01FA09
Indapres® SR	indapamide	1,5	tablets with modified release	C03BA11
Klacid® MR	clarithromycin	500	tablets with modified release	J01FA09
Rapten Duo	diclofenac	75	tablets with modified release	M01AB05
TAMLOS®	tamsulosin	0,4	capsules with modified release, hard	G04CA02
Tamsulosin PHS	tamsulosin	0,4	capsules with modified release, hard	G04CA02
Tanyz®	tamsulosin	0,4	capsules with modified release, hard	G04CA02
Tegretol® CR	carbamazepine	400	film tablets with modified release	N03AF01
Trimetazidin PharmaS	trimetazidine	35	tablets with modified release	C01EB15
Colospa® retard	mebeverine	200	capsules with modified release, hard	A03AA04
Dexilant®	dexlansoprazole	30	capsules with modified release, hard	A02BC06
Dexilant®	dexlansoprazole	60	capsules with modified release, hard	A02BC06
Diclofenac Duo	diclofenac	75	capsules with modified release, hard	M01AB05
Diclopram®	diclofenac,omeprazole	75+20	capsules with modified release, hard	M01AB55
Ketonal® DUO	ketoprofen	150	capsules with modified release, hard	M01AE03
Naklofen® duo	diclofenac	75	capsules with modified release, hard	M01AB05
Omnitus®	butamirate	20	film tablets with modified release	R05DB13
Omnitus®	butamirate	50	film tablets with modified release	R05DB14
Tamsunorm Combi®	tamsulosin,solifenacin	0,4+6	tablets with modified release	G04CA53
Valomindo®	valsartan,indapamide	160+1,5	tablets with modified release	C09DA03
Zeliftan	tamsulosin,solifenacin	0.4+6	tablets with modified release	G04CA53

Table 1. Modified release dosage forms in the Republic of Serbia

Hard capsules with modified release usually contain gelatin in their composition, which makes up the largest part of the body and cap of the capsule, then methacrylic acid-ethylacrylate copolymer (1:1) dispersion 30%, which is part of the capsule lining. Triethyl acetate is also part of the formulation that affects the plasticity of the polymer. Microcrystalline cellulose is the most widely used filler in such formulations. Hard capsules with modified release containing tamsulosin have a similar composition. The Diclofenac Duo had two types of pellets with which the capsules were filled: one type was gastro-resistant, while the other type was with a prolonged release of the active substance. Such systems are called multiparticle and can achieve zero-order release kinetics. Modified-release tablets with tamsulosin-solifenacin combination are multilayered. The first layer, for modified release, includes tamsulosin, microcrystalline cellulose, macrogol, silica, and magnesium stearate. The second layer, for immediate release, contains solifenacin, hydroxypropylcellulose, and calcium hydrogen phosphate. The coating includes hypromellose, macrogol, and dyes.
The modified-release tablets contained microcrystalline cellulose and lactose as excipients. Cross povidone and sodium starch glycolate are the most common disintegrants, while magnesium-stearate, glyceryl behenate and stearic acid are used as lubricants. In addition, standard lubricants such as talc and colloidal, anhydrous silica were included in this formulation.
The modified-release film tablet formulation consisted of materials that make up the core as well as the coating (film). The core was most often made up of matrix systems, which consisted of a hydrophilic or hydrophobic polymer. The hydrophilic polymers used were sodium alginate and sodium-calcium alginate; while ethyl cellulose was used as a hydrophobic polymer. Filmogenic material consisted of hypromellose and Macrogol 6000. These formulations also included various colors, such as titanium dioxide (E171), iron (III) oxide (E172), cochineal red (E124). Croscarmellose sodium was often used as a disintegrant.

CONCLUSION

The analysis of the data highlights the conclusion that in the Republic of Serbia there are tablets, film tablets and capsules in the form of modified release, while tamsulosin is the active pharmaceutical substance that has the most registered formulations with modified release.