

PRIMJENA AQbD PRINCIPA U RAZVOJU METODE ZA ZA SRODNE SUPSTANCIJE LOTEPREDNOL ETABONATA U GOTOVOM PROIZVODU

APPLYING AQbD APPROACH IN DEVELOPMENT OF METHOD FOR RELATED SUBSTANCES OF LOTE PREDNOL ETABONATE IN DRUG PRODUCT

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CILJ

Loteprednol etabonat (LE) retrometabolički je dizajniran kortikosteroid za lokalnu, topikalnu primjenu koji se koristi u liječenju umjerene do teške bolesti suhog oka (eng. *Dry eye disease, DED*) [1].

Za JGL formulaciju loteprednol etabonata kapi za oko, suspenzije cilj je bio razviti selektivnu metodu tekućinske kromatografije za određivanje srodnih supstancija loteprednol etabonata.

MATERIJALI I METODE

Razvoj metode proveden je kroz program Fusion QbD® koristeći principe kvalitete ugrađene kroz dizajn u analitici (eng. *Analytical Quality by design, AQbD*).

Prototip JGL formulacije cijepjen je sa 7 poznatih onečišćenja i praćeno je razlučivanje između aktivnice (loteprednol etabonata) i dodanih onečišćenja.

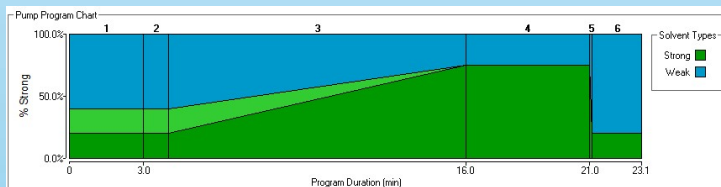
REZULTATI

SCREENING

4 kolone (Waters Acquity BEH Phenyl, CSH Fluoro Phenyl, BEH C18, CSH Phenyl Hexyl)

2 organska otapala (acetonitril, metanol)

4 vrste pufera / otopine aditiva (HCOOH, H₃PO₄, CF₃COOH, NH₄OH/HCOOH)



OPTIMIZACIJA

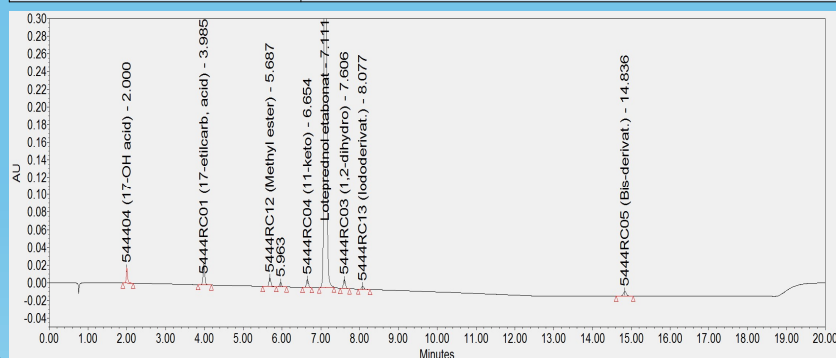
Kolona Waters Acquity BEH C18

2 organska otapala (acetonitril, metanol)

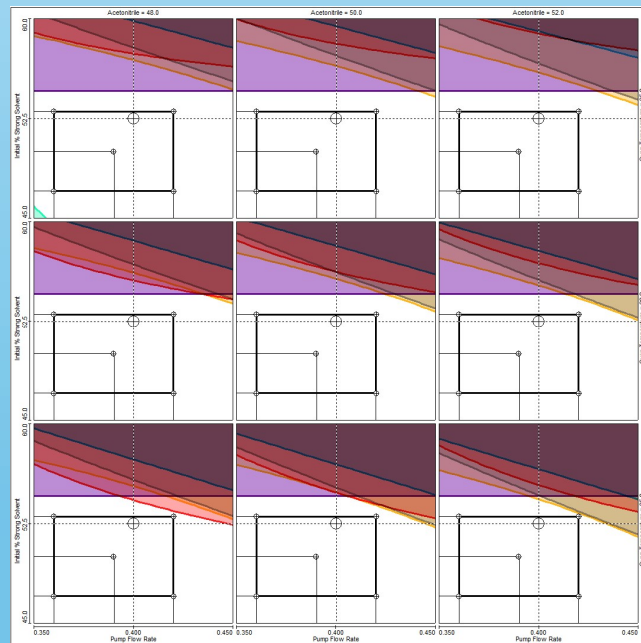
2 otopine aditiva (0.15% HCOOH i 0.15% CF₃COOH)

RAZVIJENA METODA

PROTOK	0.39 ml/min					
DETEKTOR	λ=244 nm					
VOLUMEN INJEKTIRANJA	3 µl					
TEMPERATURA AUTOSAMPLERA	4 °C					
KOLONA	Acquity UPLC BEH C18 100x2.1 mm I.D., 1.7 µm					
TEMPERATURA KOLONE	30 °C					
MOBILNA FAZA I GRADIJENT MOBILNE FAZE	MF A = ACN : MeOH : 0.15% HCOOH = 25 : 25 : 50 (%V/V/V)					
	MF B = ACN : MeOH : 0.15% HCOOH = 40 : 40 : 20 (%V/V/V)					
	t/ min	0	11	17.4	17.5	20
	% MF A	100	17	17	100	100
	% MF B	0	83	83	0	0
VRIJEME KROMATOGRAFI- RANJA	20 min					



MODR (Method operable design region)



Name	Goal	Lower Bound	Upper Bound	Color
No. of Peaks	Maximize	9.5		Gray
No. of Peaks > 1.50 - Resolution	Maximize	8.3		Red
Post Peak 1 - Resolution	Maximize	3.09		Blue
Max Peak 1 - Resolution	Maximize	2.53		Green
First Peak - KPrime	Maximize	0.9500		Orange
Last Peak - KPrime	Minimize		24.1180	Teal
No. of Peaks > 2.00 - Resolution	Maximize	8.0		Purple
First Peak - Height	Maximize	16.882		Light
No. of Peaks > 1.50 - Resolution - Cpk	Maximize	2.00		Sky
Post Peak 1 - Resolution - Cpk	Maximize	2.00		Fuchsia
Max Peak 1 - Resolution - Cpk	Maximize	2.00		Gray
First Peak - KPrime - Cpk	Maximize	1.50		Gray

LITERATURA

[1] Beckman K, Katz J, Majmudar P, Rostov A. Loteprednol Etabonate for the Treatment of Dry Eye Disease. *J Ocul Pharmacol Ther.* 2020 Sep;36(7):497-511.