ICH Validated Spectrophotometric Assay of Two Quinolones with Dexamethasone in Pharmaceutical Eye Drops containing Benzalkonium Chloride as Preservative (PC-03)

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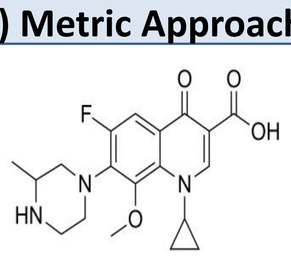
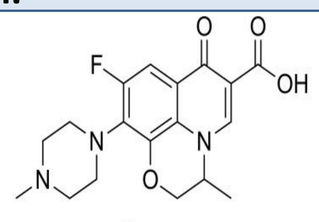
Abstract

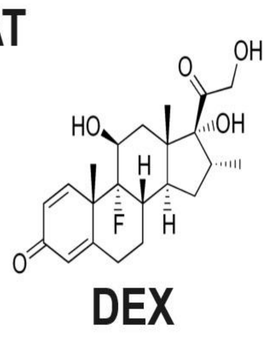
Pharmaceutical antibiotic eye drops are frequently used for eye infections or post-operative as prophylaxis. Quinolones are widely prescribed for both ear and eye bacterial infections in combination with a corticosteroid acting as an anti-inflammatory to relief the inflammation, redness, swelling and itching accompanying the infection. In the international market, dexamethasone combination with Gatifloxacin or Ofloxacin is widely used in ophthalmic solutions for treatment of ocular bacterial conditions. Meanwhile, these multi-dose ophthalmic preparations require preservation to maintain their sterility. Thus, Benzalkonium chloride is commonly added to these pharmaceutical drops as a preservative. Besides its bactericidal activity, it may act as a corneal penetration enhancer for the co-formulated drugs. This work shows direct and derivative ratio spectrophotometric methods for the determination of these two binary mixtures in the presence of benzalkonium chloride without any interference. The methods were fully validated according to the International Conference on Harmonization (ICH) guidelines. The reliability and analytical performance of the proposed procedures were statistically validated with respect to linearity, range, precision, accuracy, selectivity and detection & quantitation limits. Linear regression lines were obtained yielding high correlation coefficient values (higher than 0.999). Green analytical procedures are becoming very important nowadays and can be applied by using green sample pretreatment, using eco-friendly solvents and reagents, less energy consumption and short analysis time. Greenness assessment was performed by Green Analytical Procedure Index (GAPI) and Analytical GREEnness (AGREE) Metric Approach.

Mixture 1

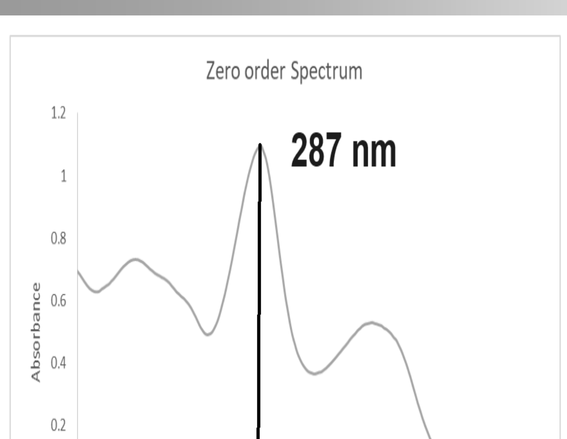


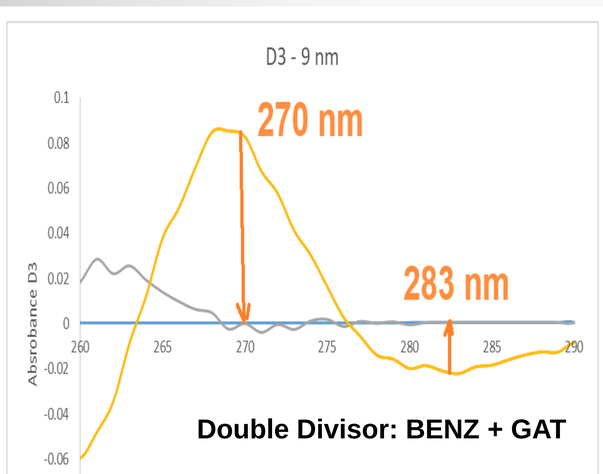


Mixture 2

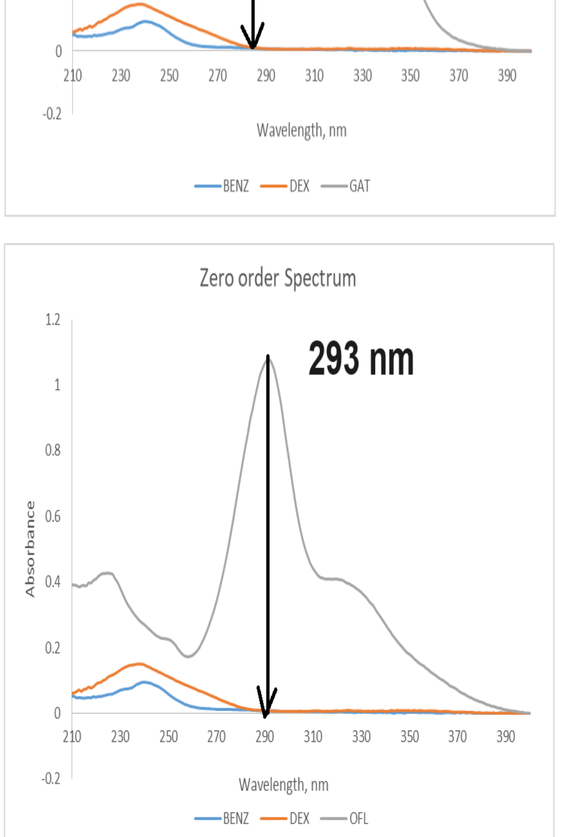


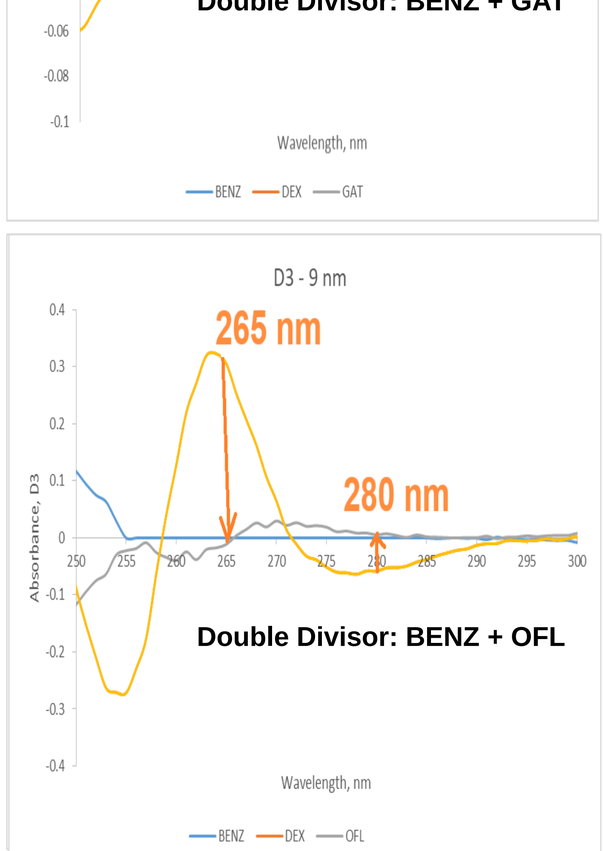
Methods





Double Divisor: BENZ + GAT





Double Divisor: BENZ + OFL

Results

Regression Analysis

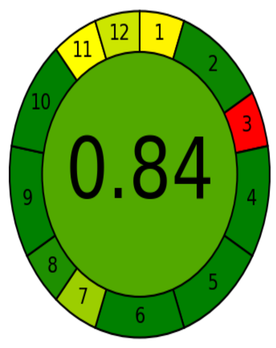
Parameter	Mixture 1		Mixture 2	
	DEX	GAT	DEX	OFL
Linearity range µg/mL	5-40	2.5-20	5-40	2-15
LOQ	4.02	2.50	3.39	1.34
LOD	1.33	0.81	1.12	0.44
Intercept, (a)	0.01	0.11	0.10	0.17
Slope, (b)	1.71×10^{-2}	6.33×10^{-2}	5.77×10^{-2}	5.93×10^{-2}
Correlation coefficient, (r)	0.9991	0.9991	0.9997	0.9996
Standard deviation of intercept, S_a	1.01×10^{-2}	1.85×10^{-2}	1.95×10^{-2}	7.93×10^{-3}
Standard deviation of slope, S_b	4.01×10^{-4}	1.51×10^{-3}	7.78×10^{-4}	9.09×10^{-4}
Standard deviation of residuals, $S_{y/x}$	1.08×10^{-2}	2.16×10^{-2}	2.10×10^{-2}	9.41×10^{-3}
F	1830.56	1766.53	5496.81	4255.62
Significance F	2.81×10^{-5}	2.96×10^{-5}	5.41×10^{-6}	7.94×10^{-6}

Accuracy and Precision (Synthetic mixtures)

Concentration (µg.mL^{-1})				Mean % Recovery RSD % E_r %			
Mix. 1		Mix. 2		Mix. 1		Mix. 2	
GAT	DEX	OFL	DEX	GAT	DEX	OFL	DEX
15	5	15	5	101.00 1.41 1.00	100.90 0.47 0.90	100.74 1.89 0.74	101.41 0.79 1.41
15	15	15	15	100.08 1.89 0.08	100.42 1.44 0.42	101.14 1.22 1.14	100.56 0.41 0.56
20	10	15	10	99.45 2.00 -0.55	99.40 1.58 -0.60	100.45 0.63 0.45	98.42 1.78 -1.58
20	5	10	5	99.40 0.74 -0.60	98.87 1.98 -1.13	98.40 1.25 -1.60	100.25 1.10 0.25
15	10	15	7	101.39 0.92 1.39	99.84 1.27 -0.16	100.31 0.33 0.31	101.84 1.64 1.84

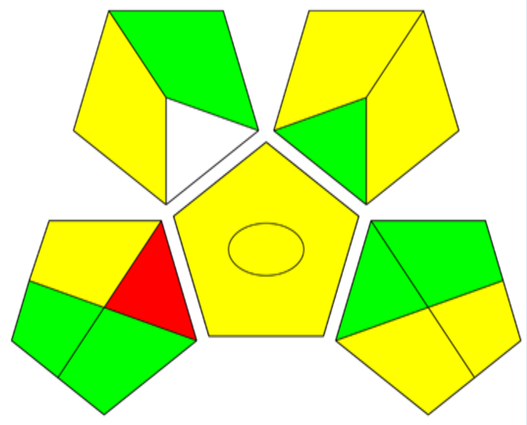
Greenness Assessment

AGREE Tool



1. Sample treatment
2. Sample amount
3. Device positioning
4. Sample prep. stages
5. Automation, miniaturization
6. Derivatization
7. Waste
8. Analysis throughput
9. Energy consumption
10. Source of reagents
11. Toxicity
12. Operator's safety

GAPI Tool



Conclusions

Simple, reliable and sustainable methods were developed for simultaneous analysis of DEX in its two binary mixtures with GAT or OFL in presence of BENZ in their ophthalmic solutions with no interference. The proposed spectrophotometric methods were able to determine both drugs in each mixture in their challenging dosage form ratio especially DEX being the minor component with minor mathematical manipulation. The developed spectrophotometric methods were validated according to the ICH and also assessed for their Greenness to prove their applicability and validity as well as being environmental friendly.

References

- **Scoper SV. Review of third-and fourth-generation fluoroquinolones in ophthalmology: in-vitro and in-vivo efficacy. Adv Ther. 2008, 25(10):979-94.**
- **Saad MN, Essam HM, Elzanfaly ES, Amer SM. Economic chromatographic methods for simultaneous quantitation of some fluoroquinolones and corticosteroids present in different binary ophthalmic formulations. Journal of Liquid Chromatography & Related Technologies. 2020, 43(7-8):271-81.**
- **Pena-Pereira F, Wojnowski W, Tobiszewski M. AGREE—Analytical GREEnness Metric Approach and Software. Analytical chemistry. 2020, 92: 10076-10082.**
- **Płotka-Wasylka J. A new tool for the evaluation of the analytical procedure: Green Analytical Procedure Index. Talanta. 2018, 181: 204-9.**