Estimation of passive gastrointestinal absorption of selected dual COX-2 and 5-LOX inhibitors using biopartitioning micellar chromatography

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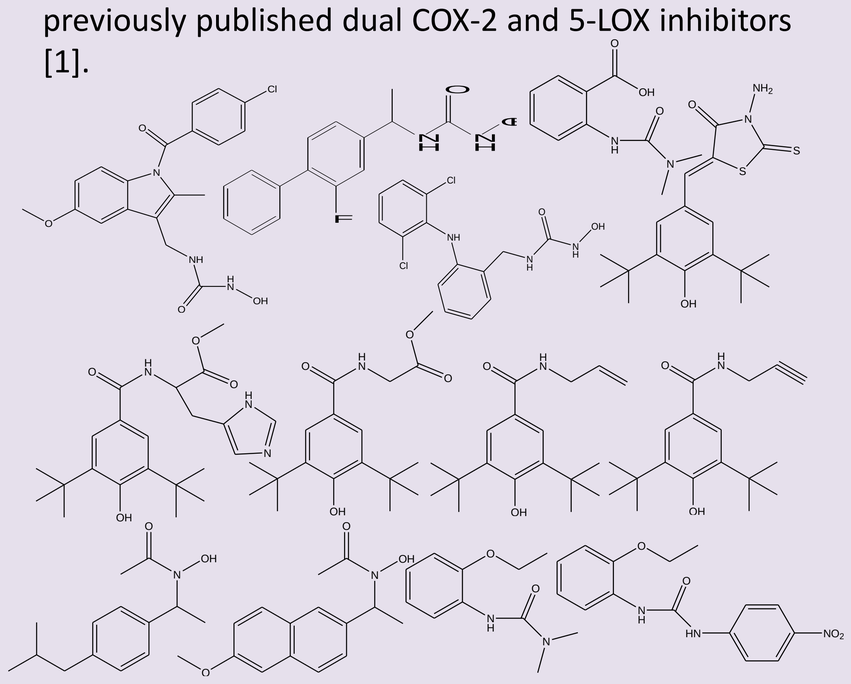
INTRODUCTION

Biopartitioning micellar chromatography (**BMC**) was used to predict passive gastrointestinal absorption of previously published dual COX-2 and 5-LOX inhibitors [1].



RESULTS

For all the tested compounds, effective lipophilicity coefficients (**logD**) were predicted at pH 5.5 using MarvinSketch 21.4 [2] and retention factors (**k**) were calculated.

Retention factors were in the range from **0.92** to **36.96**.

Compounds	k	logD (pH =5.5)
IND-NHU	**9,50**	2,15
FLU-NHU	**5,55**	2,75
DIKLO-NHU	**9,33**	2,8
BHTK-MHIS	**2,63**	2,25
BHTK-MGLY	**8,27**	3,49
BHTK-AA	**12,99**	4,65
BHTK-PA	**12,32**	4,19
2A	**2,17**	1,68
2D	**0,92**	-0,21
QSAR17	**19,96**	3,55
IBU-Ac	**3,03**	2,78
NAP-Ac	**3,02**	1,94
BHTA-3AR	**36,96**	5,21

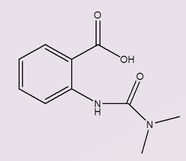
EXPERIMENTAL

Instrument: Agilent 1200 Series;

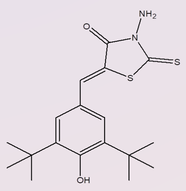
Column: ZORBAX Extend-C18 Analytical, 4.6 × 150 mm 5-Micron;
Mobile phase: aqueous phase (40 mmol/l solution of BRIJ35 in 7 mmol/l disodium hydrogen phosphate) and acetonitrile (70:30, v/v) adjusted to 5.5 by phosphoric acid;
Temperature: 36.5 °C;
Flow rate: 1 ml/min;
UV/VIS detection: 254 nm, 240 nm and 400 nm;

All tested compounds were injected in duplicates.

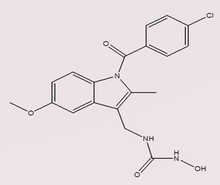
CONCLUSION

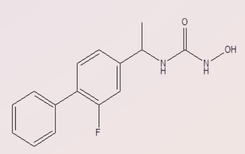


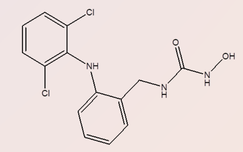
The lowest k value (0.92) - the lowest passive gastrointestinal absorption can be expected.
Low lipophilicity of this compound (logD = - 0.21) is due to the presence of carboxylic acid group, which is ionized at pH 5.5.



The most lipophilic compound (logD = 5.21) - highest k value (36.96) - the highest passive gastrointestinal absorption can be expected.







The most promising dual COX-2 and 5-LOX inhibitors had high k values (9.50, 5.55 and 9.33) – high gastrointestinal absorption can be expected.

Obtained results prove the relation between lipophilicity and retention in the applied BMC model.

REFERENCES

[1] Bošković, J.; Dobričić, V.; Mihajlović, M.; Kotur-Stevuljević, J.; Čudina, O. Synthesis, Evaluation of Enzyme Inhibition and Redox Properties of Potential Dual COX-2 and 5-LOX Inhibitors. Pharmaceuticals 2023, 16 (4), 549.
[2] MarvinSketch 21.4. *ChemAxon*, Budapest, **2021**. https://chemaxon.com/.

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