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BOOK OF THE ABSTRACTS

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Poster communication 5 – WG 1

RP-HPLC evaluation of lipophilicity of a series of dual DNA gyrase and topoisomerase IV inhibitors

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In this study, lipophilicity of twenty-three DNA gyrase and topoisomerase IV ATPase inhibitors was estimated at two pH values (5.5 and 7.4) using reversed-phase high-performance liquid chromatography (RP-HPLC) [1,2]. Retention behavior was tested on HP 1100 HPLC chromatograph, using column Zorbax Eclipse Plus C8 (150 X 4.6 mm, 5 µm particle size). Mobile phase consisted of acetonitrile and phosphate buffer (pH was adjusted to 5.5 or 7.4). Each compound was tested in four different ratios of acetonitrile and buffer (acetonitrile ranged from 20% to 65%). Column temperature was 25 °C, flow rate 1 mL/min, injection volume 20 µL and detection was performed at 254 nm. For each compound, capacity factor (*k*) was calculated and *logk* values were plotted against percentage of acetonitrile. Finally, following chromatography parameters were calculated: $logk_w$ (y-axis intercept), *a* (slope) and ϕ_0 ($-logk_w/a$).

Derivatives with the highest lipophilicity were TEL-28 and NDL-20, whereas NZ97 had the lowest lipophilicity (at both pH values, Figure 1). The majority of compounds possess similar or slightly different lipophilicities at both pH values, but the highest differences were observed for TAZ-7, LMD-17 and NCH-4d, which could significantly affect their biological properties (particularly gastrointestinal absorption, distribution and biological activity).

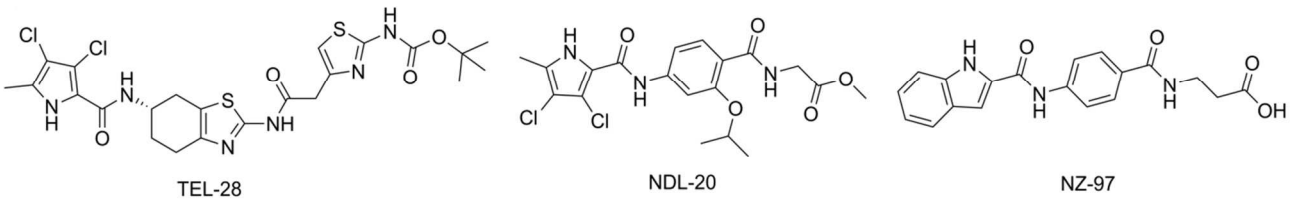

Figure 1: Chemical structures of underlined compounds

References

[1] Pallicer, J. M.; Sales, J.; Roses, M.; Rafols, C.; Bosch, E. Lipophilicity assessment of basic drugs (log Po/w determination) by a chromatographic method. *J.Chromatogr.A*, **2011**,1218, 6356-68.

[2] Han, S.-Y.; Qiao, J.-Quin.; Zhang, Y.-Y.; Yang, L.-L.; Lian, H.-Z.; Ge, X.; Chen, H.-Y. Determination of n-octanol/water partition coefficient for DDT-related compounds by RP-HPLC with a novel dual-point retention time correction. *Chemosphere*, **2011**, *83*, 131-6.