A CORRELATION OF PHYSICOCHEMICAL PROPERTIES OF SELECTED MEDICINAL COMPOUNDS TO THEIR ANATOMICAL THERAPEUTIC CHEMICAL CLASSIFICATION

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Introduction

The Anatomical Therapeutic Chemical (ATC) classification system managed by the World Health Organisation is nowadays considered the most widely recognized drug classification system.[1] Identification of rules defining classification at the molecular level as per the ATC classification system would prove beneficial for further medicinal substances development. Nevertheless, such studies are seldom found in the literature, and thus although mapping of ATC codes would provide beneficial information, the process is a challenging one.[2] The aim of the study was to assess whether common physicochemical profiles exist for compounds classified within the same ATC sub-groups.

Methodology

Eighteen level 4 sub-groups of the ATC classification system were chosen as part of the study, resulting in 9 out of the 14 main ATC classes being investigated. The study was limited to small molecules and excluded combination medicinal products. For each identified medicinal substance physicochemical parameters were generated using computational methods. Density and parachor were generated using ChemSketch (*Advanced Chemistry Development Inc., ACD/Labs*), total surface area (TSA), polar surface area (PSA) and log P were obtained using Marvin Sketch (*ChemAxon*), while aqueous solubility was computed using EPI Suite (*Environmental Protection Agency*). The generated physicochemical data was statistically assessed using Principal Component Analysis (PCA).

Results & Discussion

The results obtained indicate that a physicochemical classification of medicinal products that matches the ATC classification is plausible, revealing indicative properties of groups of compounds.

As shown in Figures 1 to 3, grouping in terms of physicochemical properties was identified for 13 ATC sub-groups out of the total of 18 sub-groups investigated. This was observed both for ATC groups consisting of molecules having closely related chemical structures, such as the bisphosphonates (M05BA) and the plain ACE inhibitors (C09AA), as well as for groups containing diverse molecules, such as the other antiepileptics (N03AX) and the other antidepressants (N06AX). Moreover, this clustering in turn highlighted specific physicochemical properties particular to each group of molecules' position on the plot.

Such an approach may be useful as a predictive tool in identifying a potential ATC classification of lead compounds as well as potential investigation for alternate indications for drugs already approved on the market, based on their physicochemical properties .

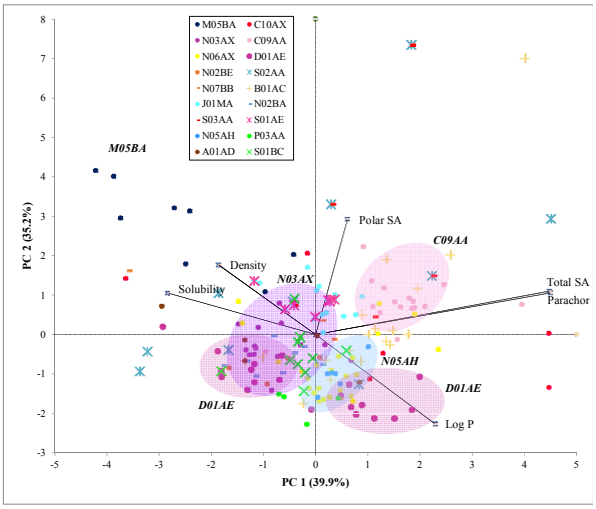

Figure 1: PCA plot representing clustering for sub-groups M05BA, C09AA, D01AE, N05AH and N03AX

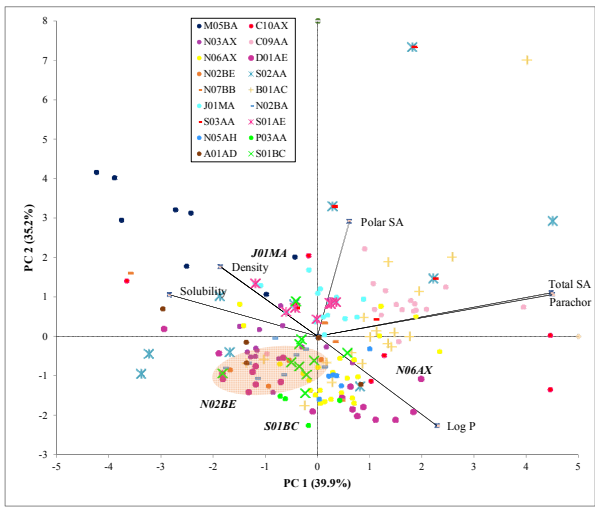

Figure 2: PCA plot representing clustering for sub-groups N02BE, J01MA, S01BC and N06AX

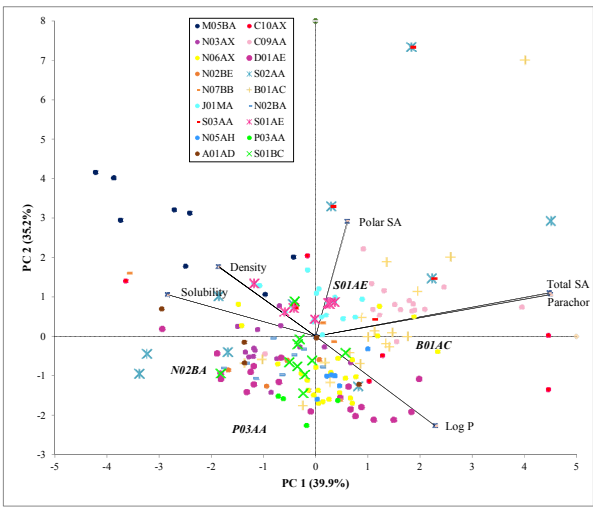

Figure 3: PCA plot representing clustering for sub-groups P03AA, B01AC, N02BA and S01AE

References

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