APPLICATION OF BOTH, CLUSTER AND PRINCIPAL COMPONENT ANALYSIS FOR EVALUATION THE LIPOPHILICITY PARAMETERS OF SELECTED ANTIANDROGEN DRUGS

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ABSTRACT

One of the most important physicochemical parameter determining the activity and toxicity of substances is lipophilicity [1]. It affects the bioavailability of the drug and its solubility in body fluids. The lipophilicity parameter is an important factor investigated when new drugs are designing. One of the most popular methods used to determine lipophilicity are reversed-phase thin layer chromatography (RP-TLC) and high performance liquid chromatography (RP-HPLC). Another frequently used methods are computer algorithms [2]. The subject of the research were substances belonging to the group of antiandrogens: abiraterone, bicalutamide, flutamide, nilutamide, leflunomide, teriflunomide and ailanthone. They are used to treat prostate cancer. There is a big need to find quick, simple and efficient tools for assessing the lipophilic properties of drugs and their candidates. Such tools include for example statistical analysis of CA (Cluster Analysis) and PCA (Principal Component Analysis). CA analysis is a statistical method of grouping items into relatively homogeneous classes. PCA, on the other hand, is about increasing the interpretation of data while maintaining the maximum amount of information. It allows you to reduce the dimensionality of the statistical data set.

METHODS AND MATERIALS

The lipophilicity parameters of the tested compounds were obtained in the form of R_{MW} values by using thin layer chromatography (RP-TLC) under different mobile phases: ethanol-water (EtOH/H_2O), propan-2-ol-water (P-2-ol/H_2O) and acetonitrile-water (ACN//H_2O) on the following chromatographic plates: $RP2F_{254}$, $RP18F_{254}$ and $RP18WF_{254}$. Theoretical values of logP were predicted by calculation methods (AlogPs, AClogP, AlogP, MlogP, xlogP2, xlogP3) [2]. In addition to this the selected physicochemical properties of examined compounds such as density, boilling point, molar refractivity, polar surface, molar volume, polarizability obtained from data base chemspider were compared [3]. The applied CA and PCA analysis allowed for the comparison of the tested compounds depending on their lipophilicity parameters determined by the RP-TLC method and the calculated logP values as well as other physicochemical parameters.

AIM OF THE WORK

The aim of this study was to use both methods, i.e. Cluster Analysis (CA) and Principal Component Analysis (PCA) to assess the lipophilicity of selected antiandrogen substances such as abiraterone, bicalutamide, flutamide, nilutamide, leflunomide, teriflunomide and ailanthone. In the presented work, we used the both methods to compare the selected physicochemical properties includes the lipophilicity of seven antiandrogens with different chemical structures – Fig.1.

RESULTS

The discussed lipophilicity parameters i.e. theoretical partition coefficient designated as logP values and chromatographically obtained lipophilicity parameter in form of R_{MW} values for all studied compounds were compared by using CA and PCA analysis. An exemplary dendrograms of CA are shown in Fig. 2 and 3. Figure 2 shows the results of CA of chromatographic lipophilicity parameters and theoretical logP values of studied compounds. Next dendrogram presented in Fig. 3 shows the results of CA of all studied antiandrogens based on obtained lipophilicity parameters.

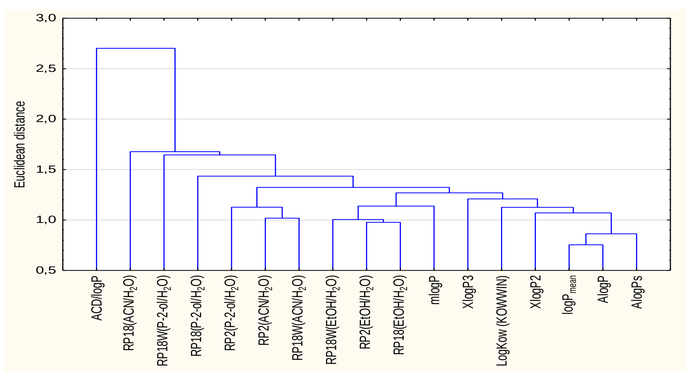

Fig. 2. Cluster analysis (CA) of chromatographic lipophilicity parameters and theoretical logP values of studied compounds.

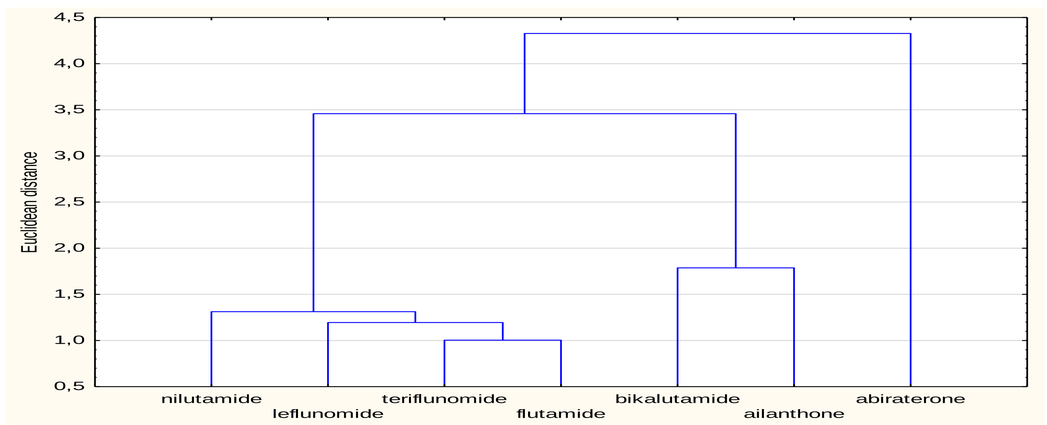

Fig. 3. Dendrogram of similarity analysis of all studied antiandrogens based on obtained lipophilicity parameters.

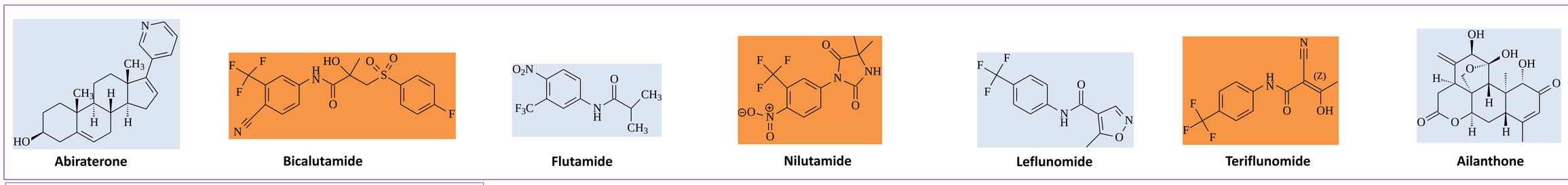

Fig. 3 Structural formulas of tested compounds.

CONCLUSIONS

Our study confirms the usefulness of both methods, i.e. CA and PCA, to assess the lipophilicity of the tested bioactive compounds belonging to antiandrogen drugs. Fig. 3 shows similarity of all examined compounds on the basis of their lipophilicity parameters. Similar results were obtained during the CA analysis of other physicochemical parameters of tested compounds. Of all lipophilicity parameters, the biggest similiarity was observed between the mean value of theoretical logP and AlogP as well for R_{MW} values obtained on both i.e. RP2 and RP18 plates by using EtOH-water as mobile phase. The presented results can be important in design of new formulations of studied compounds or new drug candidates.

References

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