Title: Lipophilicity Estimation of Statins as a Decisive Physicochemical Parameter for Their Hepato-Selectivity Using Reversed-Phase Thin Layer Chromatography

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Lipophilicity plays a crucial role in determining the hepato-selectivity and hence, the biological activity and the associated side effects of statins. Herein, the employment of RP-TLC for estimation of lipophilicity of six statins namely; atorvastatin, simvastatin, pravastatin, lovastatin, rosuvastatin and fluvastatin is examined. A very good correlation between the chromatographically-determined retention parameters (relative lipophilicity (RM₀) or lipophilic parameter (C₀)) and both experimental and computed log P values were obtained. However, the results indicate that the type of organic modifier in the mobile phase system (methanol, acetonitrile and acetone) has a small influence on RM₀ or C₀ values. Higher values of RM₀ or C₀ are ascribed to lipophilic statins and lower values of RM₀ or C₀ are attributed to hydrophilic ones. Therefore, RM₀ or C₀ could be effectively used as simple practical predictors of extra-hepatic distributions of statins and thus their expected side effects. Furthermore, three QSPR (quantitative structure-property
relationship) models were constructed to describe the relationship between $R_{MO}$ with log P and log D of the statins under investigation. These models can be very useful to predict the lipophilicity of other members of statin drugs and might be expanded to newly synthesized compounds with the same structural features.

**Keywords:**
Reversed-phase thin layer chromatography, Relative lipophilicity, Statins, Hepato-selectivity, Quantitative structure-retention, relationship (QSSR), Quantitative structure-property, relationship (QSPR)