Adsorption of the model drug testosterone on laboratory tips

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Introduction

Quantitative drug analysis requires careful evaluation of each step of the process, including liquid handling. Loss by adsorption is an analytically problematic issue, especially for hydrophobic compounds like testosterone. Therefore, we investigated the operational adsorption characteristics of this steroid in different solvents and using different laboratory tips. In addition, the adsorption characteristics of 6 other steroids were investigated and initial QSPR established.

Experimental

Solvent: 10mM phosphate buffered saline (PBS), 5% bovine serum albumin (BSA) in PBS and AcCN/H 2O (50/50, V/V)

Methodology:

- Plastic: untreated standard PP tips (3 different suppliers), siliconized, developmental (proprietary) NO:1 to NO:5
- Resulting solution HPLC: 
  - Isocratic AcCN/H 2O (HCOOH 0.1% m/V)
  - UV detection

Results and discussion

1. Influence of BSA and organic modifier AcCN in solvent (untreated plastic tips)

- Protocol is adequate to significantly detect adsorption phenomena.
- Solvent plays important role: BSA and AcCN containing aqueous solutions did not exhibit adsorption at all.
- Testosterone dissolved in PBS shows a significant adsorption.
- Overall, molecular volume (V, AMR) and hydrophobicity (AlogP modulated by Hy, nH) positively influence adsorption. Basic hetero-atoms (B, Ms) oppositely decreases adsorption.

2. Influence of laboratory tip (PBS solution)

- Difference between investigated materials is observed.
- Glass shows negligible adsorption, untreated plastic laboratory-tips the highest adsorption.
- Other tips behave between these two extremes.

3. Other Steroids

Mean adsorption values are presented in Figure 3 resulting in different classes:
- PBS/PP tips: mean adsorption values on PP tips of three different suppliers.
- PBS/glass: adsorption on glass tips in PBS.
- Others: mean adsorption on PP tips of three different suppliers and on glass in 5% (m/V) BSA and AcCN/H 2O 50/50 (V/V).
- Overall experimental error: Standard deviation over all “others” values = 1.8% (n = 53)

QSPR using MLR resulting in significant descriptors:

1) LFER (Abraham) descriptors: - McGowan characteristic volume (V) - Solute H-bond basicity (B)
2) Constitutional descriptors: - Number of H-atoms (nH) - Mean electrotopological state (Ms)
3) Molecular descriptors: - Ghose-Crippen molar refractivity (AMR) - Ghose-Crippen octanol-water partition factor coefficient (AlogP) - Hydrophilic factor (Hy)

Table 1: Recovery of testosterone glass vs. PP tips, PBS vs. AcCN/H2O (%)

Table 2: QSPR models

Conclusions

1. Significant adsorption of testosterone in PBS on untreated laboratory plastic tips; less adsorption on developmental tips.
2. No significant adsorption of testosterone in BSA or AcCN containing solutions on any investigated tip types.
3. Above conclusions also for other steroids to different extent; 4 groups: 1) Triamcinolone: no biopharmaceutical significant adsorption (4.8% ± 0.5%, n = 3) 2) Dexamethasone, corticosterone, triamcinolone-acetonide, testosterone (15.7% ± 2.7%, n = 12) 3) Progesterone (26.2% ± 2.1%, n = 3) 4) Hydrocortisone 21-octanoate ( = 68.1% ± 12.9%, n = 3)
4. QSPR established by LFER, constitutional and molecular descriptors: 1) Large V-coefficient: greater dispersion force interaction and higher energy required size cavity. 2) Increase in H-bond basicity decreases the plastic-tip interaction. 3) The number of hydrogens positively influences the adsorption (e.g. hydrophobic, as more carbons) 4) The higher the polarizability (expressed as Ms) often due to more polar hetero-atoms, the lower the adsorption. 5) Higher hydrophobicity (AlogP) corresponds with higher adsorption, which is fine-tuned by the opposite hydrophilicity factor (Hy). 6) A positive effect of the Ghose-Crippen molar refractivity (AMR) gives a positive adsorption.

Overall, molecular volume (V, AMR) and hydrophobicity (AlogP modulated by Hy, nH) positively influence adsorption. Basic hetero-atoms (B, Ms) oppositely decreases adsorption.