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Evaluation of adsorption of various analytes in cerebrospinal fluid

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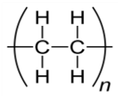
Introduction

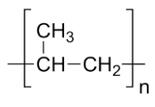
For **drug development**, the concentration of the compounds need to be measured in fluids e.g. plasma, urine, **cerebrospinal fluid (CSF**). In urine and CSF the analysis of compounds is difficult because of the risk of **adsorption** to sampling materials. For urine an additive can be added to avoid this. Because of patient safety reasons this is not allowed for CSF sampling. In addition, the concentration in CSF is often to low what makes analysing extra difficult.

Aim

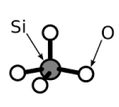
In this investigation, the impact of various materials on adsorption of the compounds during sampling and storage was evaluated. The relation between adsorption to sampling materials and the **physiochemical properties of the compounds** was evaluated to see if any predictions can be made about the amount of adsorption. Also the possibility to set up a **generic procedure** of materials with less than **15% of adsorption** was evaluated. A hypothesis is that compounds with a high log P will adsorb more to non-polar materials. For the most important materials, the composition is given:



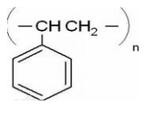
Polyethylene



polypropylene



glass



polystyrene

Materials

- Needle
- Collecting tubes
- Pipet
- Storage tubes

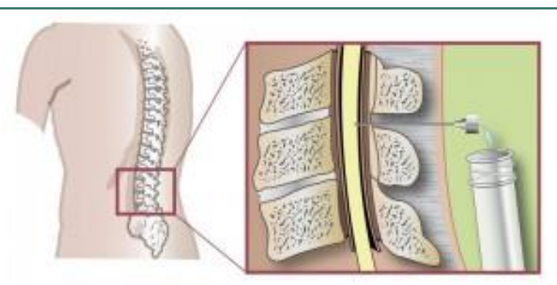
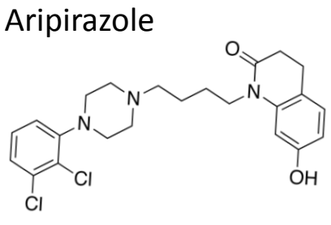


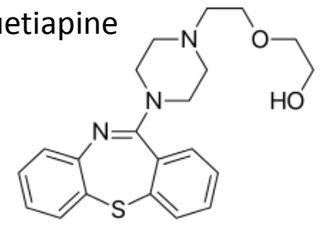
Figure 1: sampling CSF

Compounds

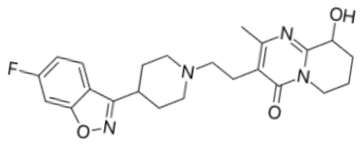
Aripirazole



Quetiapine



Paliperidone



3 Janssen compounds:

A, B, C

Methods

The analysis will be done by HPLC-MS/MS, all compounds are together in a mix

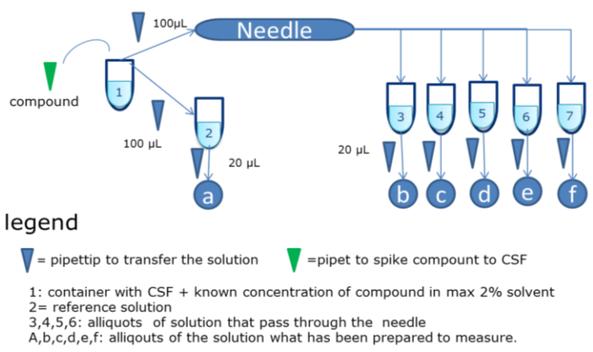


Figure 2: Test principle for needles

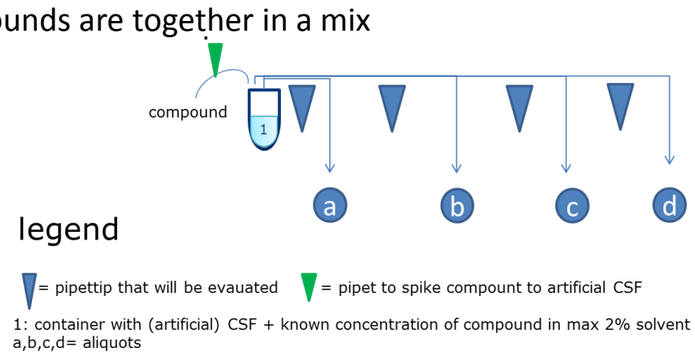


Figure 3: Test principle for pipet tips

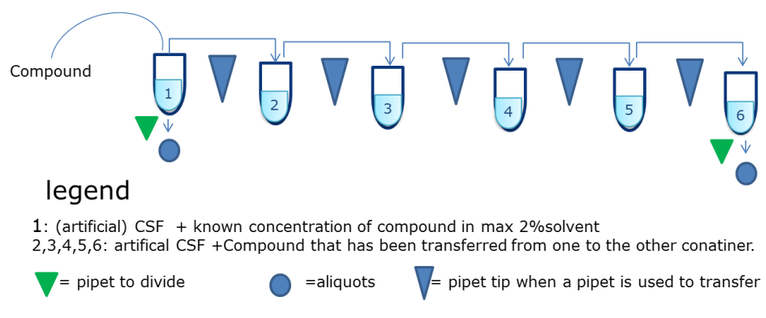


Figure 4: Test principle for tubes

Results

Table 1:Adsorption of the analytes in the different materials, qualitative (0= no adsorption , 5= >15% adsorption)

Compounds			Materials																Sum best
	log P	pKa	Needle		Collection tubes		Pipet tips							Storage tubes					
			N1	N2	C1	C2	P1	P2	P3	P4	P5	P6	P7	S1	S2	S3	S4	S5	S6	N1, C1, P1, P3 and S1
Paliperidone	1,07	4,41	0	0	0	1	1	1	1	1	2	2	2	1	0	1	0	0	0	1
Compound A	1,27	19,4	0	0	0	1	0	2	2	4	5	4	3	0	2	0	1	0	1	2
Compound B	2,98	11,02	0	0	1	1	2	1	2	2	3	2	2	1	1	1	1	1	1	3
Quetiapine	2,99	5,87	0	0	0	1	0	0	0	0	1	0	0	1	1	1	1	1	1	1
Compound C	4,86	12,85	0	0	1	1	1	2	2	3	4	3	3	1	2	2	2	3	3	3
Aripiprazole	5,31	4,29	0	0	1	1	1	2	1	5	4	1	4	1	2	2	2	3	3	4

N1= Pecan needle, N2= Spinocath, C1= Falcon tube, C2= Sarstedt tube, P1= Sarstedt pipet, P2= repeating pipet, P3= Gilson pos. displacement pipet, P4= Eppendorf Pos. diplacement pipet, P5= Eppendorf air column pipet, P6= Low retention, P7= Low binding , S1= Fluidx, S2= Micronic, S3=2 ml Sarstedt tubes, S4=0,5 ml Sarstedt tubes, S5= lo bind DNA Eppendorf, S6= lo bind protein Eppendorf; All values are for 1 transfer.

Discussion

The amount of **adsorption** in the sample stages is not that much. With the **pipet tips** used in the lab the most adsoprtion is detected. The Sarstedt pipet is a pipet used in clinics to aliquot the samples. When the adsoprtion in the **whole procedure** is calculated with the best materials, the **adsorption remains within the 15% limit** for the chosen compounds**.**

Conclusion

From the results it was concluded that the choice of material really can help to limit adsorption. However, it is not possible to completely avoid adsorption for all compounds. It was also clear that log P is not the only physicochemical parameter to predict adsorption. To predict adsorption and setting up an generic procedure more research is needed.

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janssen PHARMACEUTICAL COMPANIES OF Johnson&Johnson

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