URINARY PROFILES OF MONOHYDROXYLATED METABOLITES OF POLYCYCLIC AROMATIC HYDROCARBONS IN DIFFERENT INDUSTRIAL ACTIVITIES

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MOTIVATIONS AND OBJECTIVES

- PAHs ubiquitous in the environment
- Present in numerous workplaces
- Importance of characterization of exposure for prevention
- Biomonitoring is complementary to monitoring of ambient air.
- 1-OH-pyrene, is the metabolite the most used for routinely estimation of internal exposure to PAH,
- But Pyrene is not a carcinogen (underestimation of carcinogenic risk?),
- Other biomarkers have been proposed for biomonitoring

Aim of the study :

- To evaluate the current levels of exposure to PAHs in different industrial activities, using air sampling and simultaneous analysis of several PAHs monohydroxy metabolites in urines
- To compare the profiles of exposure
- To evaluate the influence of individual factors (smoking, genetic polymorphism) on metabolites levels

METHOD

- Cross sectional study
- Study population : 125 male workers
  - aged: 21-57, average : 41
  - 45% of smokers
- Industrial sectors and Activities
  - Coke production (n=45)
  - Aluminium production (n=20)
  - Glass production (n=15)
  - Landscape service activities (two stroke engine utilisation) (n=15)
  - Metal machining industry (mineral oil exposure) (n=30)

METHOD

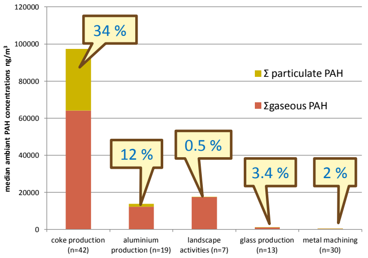
- Exposure assessment
  - ***External PAH exposure :***

    personal air sampling during the shift : 16 EPA-PAHs (vapours and particulate bound PAHs) collected on biphasic systeme (filters and XAD-2 sorbent)
  - ***Internal PAH exposure :*** Urinary spot samples collected at the end of shift (ES)and 16 hours later (ES+16).

    Monohydoxymetabolites, analysed by LC-MS/MS and HPLC-Fluorescence detection : 2-,3-&1-,4-,9-hydroxyphenanthrenes (Σ -OH-phen), 1-hydroxypyrene (1-OH-pyr), 3-hydroxybenzo(a)pyrene (3-OH-B(a)P), 1-&2-hydroxynaphalenes (Σ -OH-naph), 2-hydroxyfluorene (2-OH-fluo), 3-hydroxyfluoranthene (3-OH-flua), 1-&2- hydroxybenzo(a)anthracenes (Σ -OH-B(a)A), 3-&6-hydroxychrysenes (Σ-OHchry)
- Evaluation of individual factors
  - Genetic polymorphism in the genes coding for enzymes involved in the metabolism of PAHs : GSTM1, GSTT1, CYP1A1, EPHX1A, EPHX1T
  - Self administered questionnaire (individual protections, smoking habits, food ...)

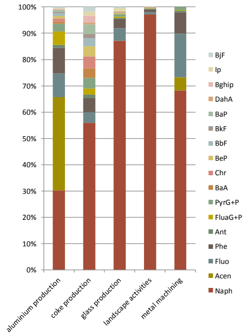
RESULTS

EXTERNAL DOSE ASSESSMENT : AIRBORNE PERSONAL SAMPLING



- The highest median airborne level of total PAH → coke production
- The proportion of particulate PAH depends on the sector of activity

EXTERNAL EXPOSURE ASSESSMENT : PROFILE OF 16 EPA-PAH IN DIFFERENT INDUSTRIAL ACTIVITIES



- Very different profiles of PAH
- Gaseous PAH always majoritary: naphtalene, acenaphtene, fluorene

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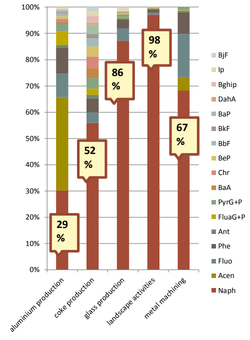

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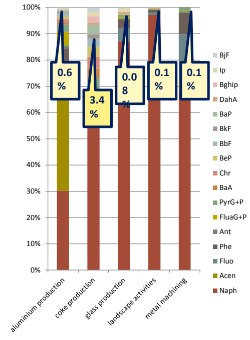


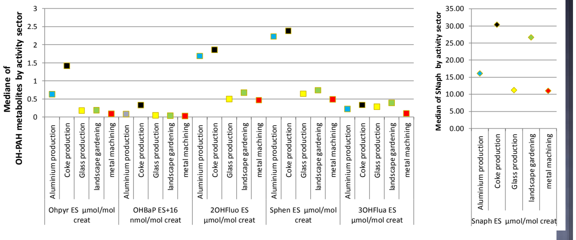
- Very different profiles of PAH
- Gaseous PAH are always majoritary: but differences of proportion between activities : exemple for naphtalene…
- For particulate PAH the highest levels are present in coke production : exemple for BaP

INTERNAL EXPOSURE ASSESSMENT : URINARY HYDROXYLATED METABOLITES

- Métabolites detection
  - OH-metabolites are detected on 75 to 100% of the samples
  - except for : ΣOH-Chry, 1 and 2OH-BaA

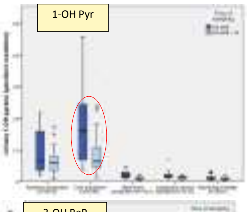
moment du prélèvement	End-Shift		End-Shift + 16			
OH-Metabolites	n	%> LOD	n	%>LOD	Analytical method	LOD (ng/L)
1OHPyr	116	100,0	114	99,1	HPLC-Fluo	20
3OHBaP	91	77,8	89	76,7	HPLC-Fluo	0,06
1Naph	116	100,0	115	100,0	HPLC-Fluo	300
2Naph	116	100,0	115	100,0	HPLC-Fluo	300
ΣNaph	116	100,0	115	100,0	HPLC-Fluo	300
2OHFluo	105	89,7	110	96,5	LC-MS-MS	1,9
2, 3OHPhen	117	100,0	116	100,0	LC-MS-MS	0,3
1,4,9OHPhen	117	100,0	116	100,0	LC-MS-MS	0,2
ΣOHPhen	117	100,0	116	100,0	LC-MS-MS	0,2-0,3
3OHflua	117	100,0	116	100,0	LC-MS-MS	0,5
3, & 6 OHChry et 2OHBaA	1	0,9	3	2,6	LC-MS-MS	0,2
1OHBaA	2	1,7	7	6,0	LC-MS-MS	0,2

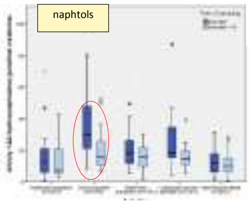
INTERNAL EXPOSURE ASSESSMENT : MEDIAN OF URINARY OH-METABOLITES BY SECTOR



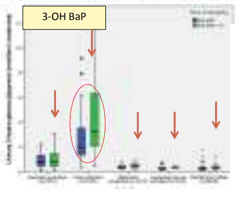
- For all metabolites, the highest median level is observed in coke production workers, followed by aluminium production workers
- In coherence with airborne level, ∑Naph is high in landscapegardeners

OH URINARY METABOLITES OF PAH BY INDUSTRIAL SECTORS : DEPENDING ON THE TIME OF SAMPLING (1)



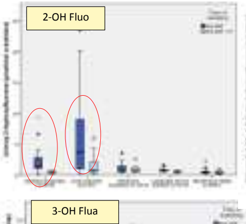


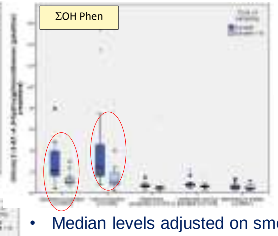
* adjusted on recent smoking



- Median levels with adjustment on smoking are higher in coke production workers
- Median urinary concentrations are higher at the end of shift, except for 3 OHBaP wich is higher at the begining of the following shift

OH URINARY METABOLITES OF PAH BY INDUSTRIAL SECTORS : DEPENDING ON THE TIME OF SAMPLING (2)





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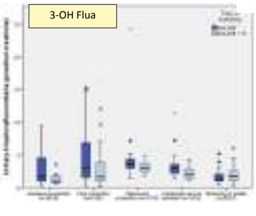


- Median levels adjusted on smoking are always higher in coke production workers and aluminium production workers except for 3OHFlua
- Median urinary concentrations are higher at the end of shift

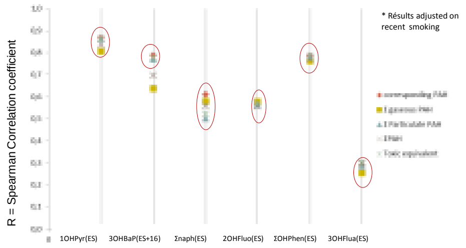
VARIATION FACTORS OF URINARY OH-PAH EXCRETION

Multivariate analysis : only factors with significant influence on metabolites excretion are presented (multiplicative factor)

	1OHPyr	3OHBap	ΣNaph	2OHFluo	ΣOHPhen	3OHFlua
Smoking (previous 8 h)	X 6.23	X 2.17	X 17.00	X 7.94	X 2.52	X 8.81
Corresponding airborne PAH level	X 7.85	X 4.98	X 3.70	X 8.79	X 5.79	X 1.54
Grilled/smoked food (previous 12 h)			X 3.13			
Contact with oils			X 2.84		X 1.77	X 3.55
Cutaneous exposure		X 2.80				
Gaz exhaust exposure				X 8.79		
No gloves protection	X 4.97					
Intense Physical activity		X 2.44		X 3.64		

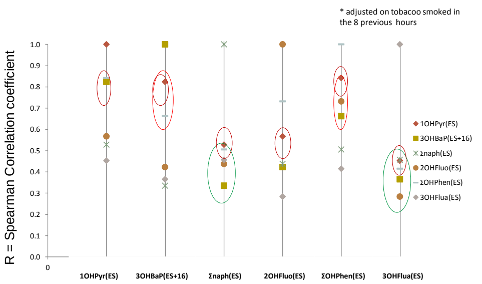
No significant impact of : genetic polymorphisme, use of protective mask

CORRELATIONS BETWEEN PAH AIRBORNE CONCENTRATION AND URINARY METABOLITES EXCRETION



- Best correlations between :
  - 1-OHpyr, Σ OH-Phen and inhaled amount of PAH : with their corresponding PAH, and also Σparticulate PAH, Σ gazeous PAH, Σ PAH, toxic equivalents
  - Between 3-OHBaP and atmospheric PAH and specially with particulate PAH
- Intermediate corrélation for 2-OH-Fluo and ΣNaph
- Bad corrélation for 3-OH-Flua

CORRELATIONS BETWEEN OH-PAH METABOLITES



- For each metabolite, the best correlation is always observed with 1-OH Pyr
- Good correlations between 1-OH pyr , 3-OH BaP and OH-Phen
- Worst correlation between naphtols, 3OH-Flua and the other metabolites

CONCLUSION

- Levels and Profiles of PAH and their metabolites are different in various industrial activities
- Metabolites with 2 and 3 cycles are more often detected (naphtols, OH-Phen, 1OH-Pyr, 2OH-Fluo, 3OH-Flua)
- Influence of smoking even at occupational exposure level
  - For all metabolites and particularly naphtols
  - Best parameter is the number of cigarettes smoked during the 8 previous hours
- Best time for urinary spot sampling : end of shift for all metabolites except for 3 OH BaP
- Metabolites best correlated together and to atmospheric concentrations
  ⇒ metabolites of Pyr, BaP, Phen

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