Comparison of the *in vivo* genotoxicity of electronic and conventional cigarettes aerosols after subacute, subchronic and chronic exposures

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INTRODUCTION

Tobacco smoking is classified as a human carcinogen. Since recent years, a wide variety of new products, in particular electronic cigarettes (e-cigs), have appeared on the market as an alternative to smoking. Although the *in vitro* toxicity of e-cigs is relatively well known, there is currently a lack of data on the long-term health effects of vaping on whole organisms.

In this context, the aim of our study was to compare the *in vivo* genotoxic and mutagenic potential of conventional cigarette and e-cig emissions after subacute, subchronic and chronic exposures. A battery of *in vivo* tests was performed in order to assess DNA damage, chromosomal aberrations, gene mutations and oxidative stress.

MATERIALS AND METHODS

Cigarette

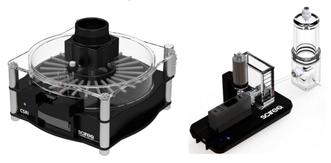
3R4F

E-cigarettes

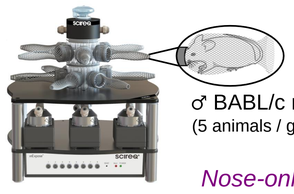
Modbox 0,5 Ω
18W and 30W
E-liquid "blond tabacco" flavour
16 mg/mL nicotine

Aerosol generations

Smoking robot
SCIREQ®, Emka tech.



System of exposure
InExpose™, SCIREQ®, Emka tech.



♂ BABL/c mice
(5 animals / group)

Nose-only exposure

Health Canada Intense puff profile:
Volume: 55 mL; Duration: 2 s, Frequency: 2/min

Treatment schedules

Subacute
4 days 30, 60, 90 min/day

Subchronic
3 months 60 min/day, 5 days/week

Chronic
6 months 60 min/day, 5 days/week

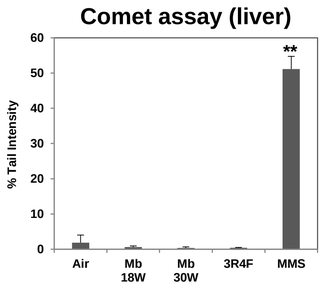
Tests performed

- **Standard comet assay** (OCDE 489) on lung, liver
- **hOGG1-modified comet assay** on lung, liver
- **Micronucleus test** (OCDE 474) on bone marrow
- ***Pig-a* gene mutation assay** on erythrocytes
- **8-OHdG assay**

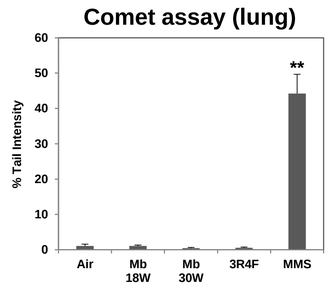
RESULTS

Subacute exposure

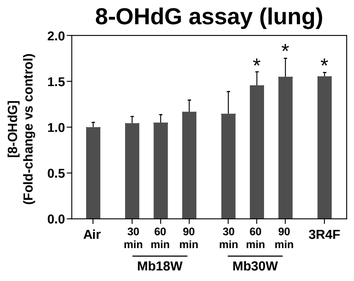
Comet assay (liver)



Comet assay (lung)



8-OHdG assay (lung)



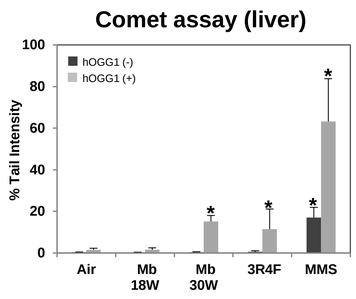
➔ No primary DNA damage on liver and lung

➔ **Mb30W** and **3R4F**: increase in oxidative DNA damage on lung

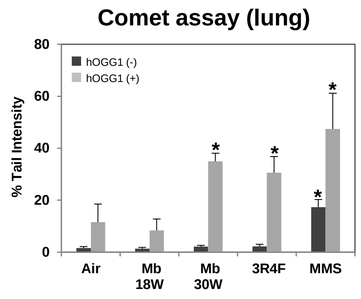
MMS: methyl-methanesulfonate * p<0.05 ** p<0.01

Chronic exposure

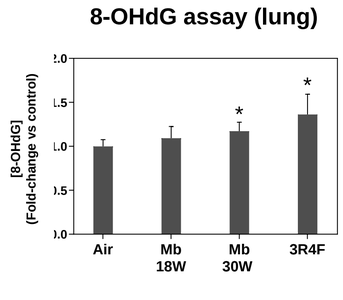
Comet assay (liver)



Comet assay (lung)



8-OHdG assay (lung)



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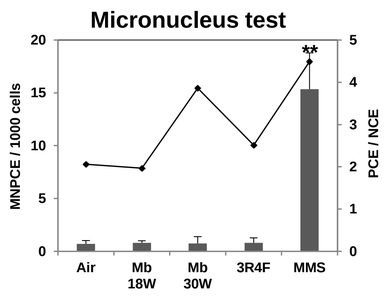
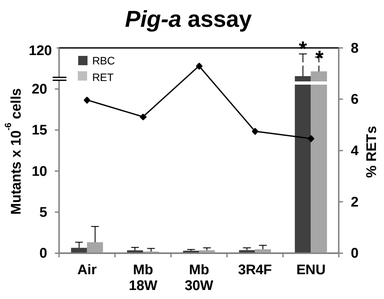
Micronucleus test



Pig-a assay



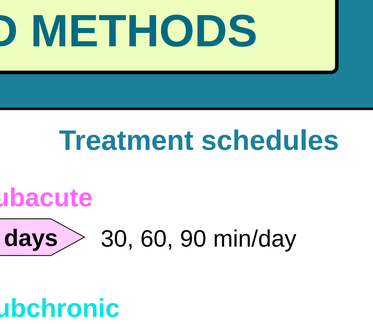
➔ No chromosomal aberrations

➔ No gene mutations

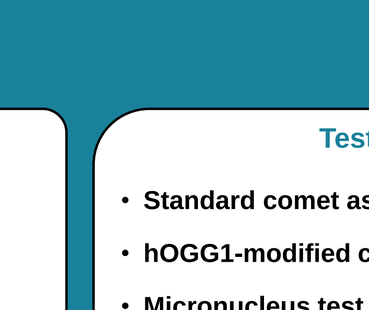
MMS: methyl-methanesulfonate
ENU: ethyl-nitrosourea
MN: micronuclei
PCE: polychromatic erythrocytes
NCE: normochromatic erythrocytes
RET: reticulocytes
REB: red blood cells
* p<0.05
** p<0.01

Subchronic exposure

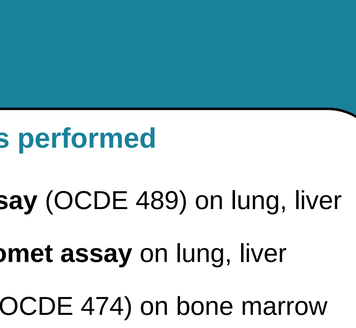
Comet assay (liver)



Comet assay (lung)



8-OHdG assay (lung)



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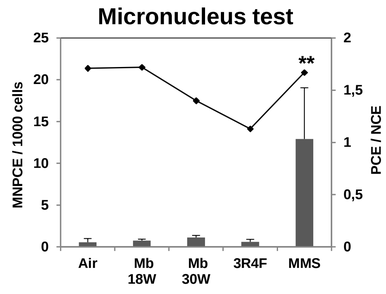
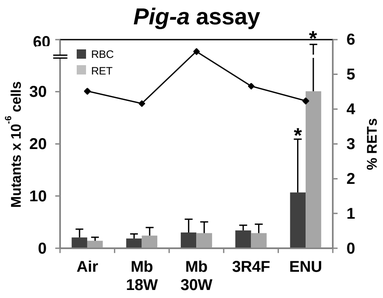
Micronucleus test



Pig-a assay



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Summary of results

	4 days			3 months			6 months		
	Mb 18W	Mb 30W	3R4F	Mb 18W	Mb 30W	3R4F	Mb 18W	Mb 30W	3R4F
Standard comet assay	-	-	-	-	-	-	-	+	+
Micronucleus test	n.a.	n.a.	n.a.	-	-	-	-	-	-
***Pig-a* assay**	n.a.	n.a.	n.a.	-	-	-	-	-	-
hOGG1-comet assay	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	-	+	+
8-OHdG assay	-	+	+	-	+	+	-	+	+

n.a.: not assessed; -: negative result; +: positive result

CONCLUSION

- **Our results show that only the high-power e-cig and the 3R4F cigarette induced oxidative DNA damage in the lung and the liver of exposed mice.**
- **In return, no significant increase in chromosomal aberrations or gene mutations were noted whatever the type of product.**
- **This study demonstrates that e-cigs, at high-power setting, should be considered, contrary to popular belief, as "hazardous products" in terms of genotoxicity in a mouse model.**

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