

5F-cumyl-PINACA in 'e-liquids' for electronic cigarettes – A new type of synthetic cannabinoid in a trendy product

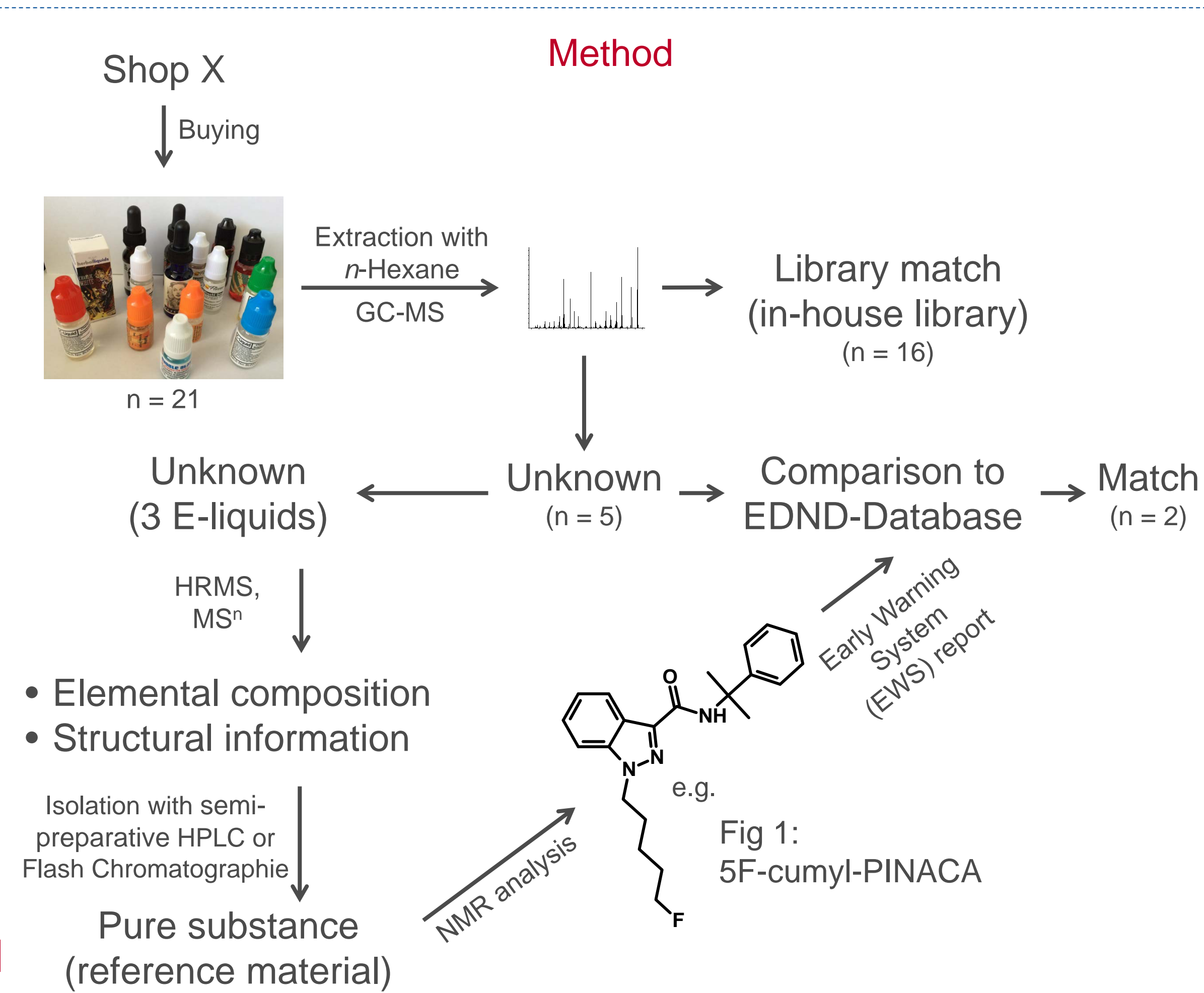
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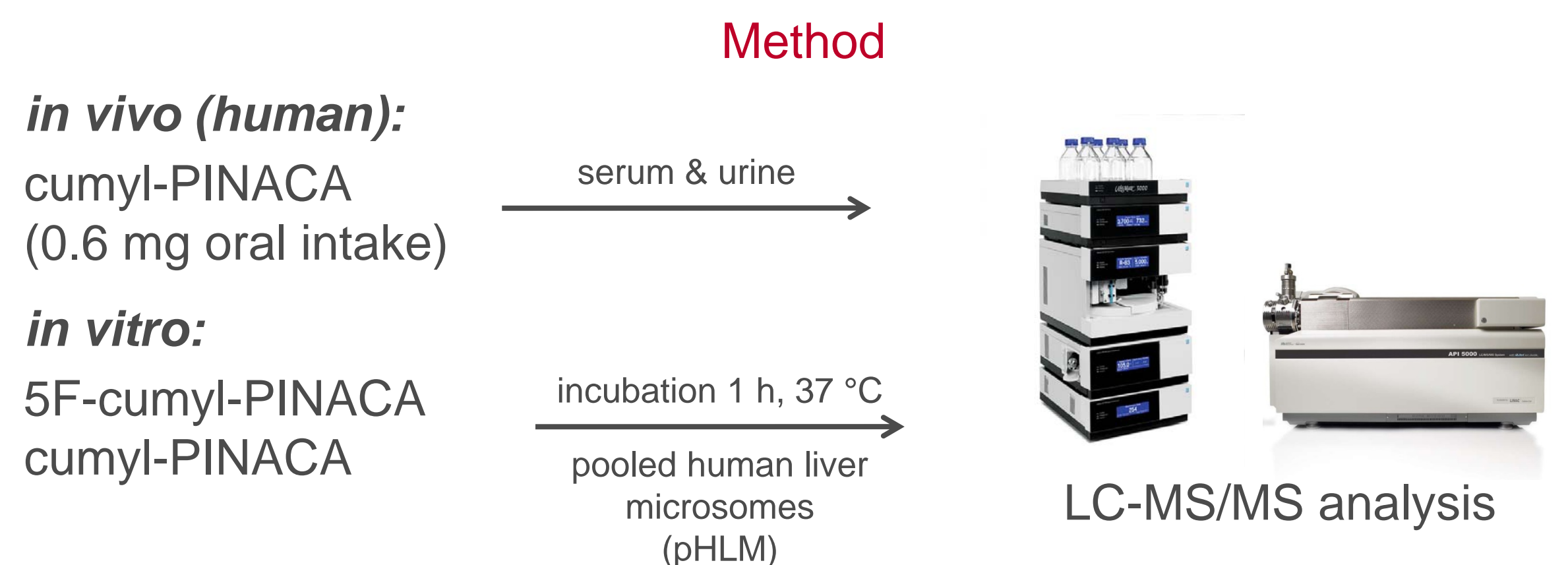
Introduction:

In recent years, e-liquids used in electronic cigarettes have become an increasingly attractive alternative to smoking tobacco. Especially among young people e-cigarettes are becoming more and more popular [1]. A new trend is the use of e-liquids containing synthetic cannabinoids instead of nicotine as active ingredients. In the frame of the EU-Projects 'SPICE', 'SPICE II Plus' and 'SPICE Profiling', which comprise a systematic monitoring of the online market of 'legal highs', e-liquids were bought from online retailers who also sell herbal blends.

Product monitoring



Metabolism



Results

After ingestion of 0.6 mg cumyl-PINACA orally, the volunteer did not experience any drug-related symptom. Cumyl-PINACA itself could be detected in serum over a period of about 17 h. The maximum concentration observed was 0.1 ng/ml (6 h after ingestion, Fig. 2). The main metabolites of cumyl-PINACA showed mono- and dihydroxylation at the pentyl moiety (*in-vivo* and *in-vitro*) and could be detected for at least 31 h (Fig.3)

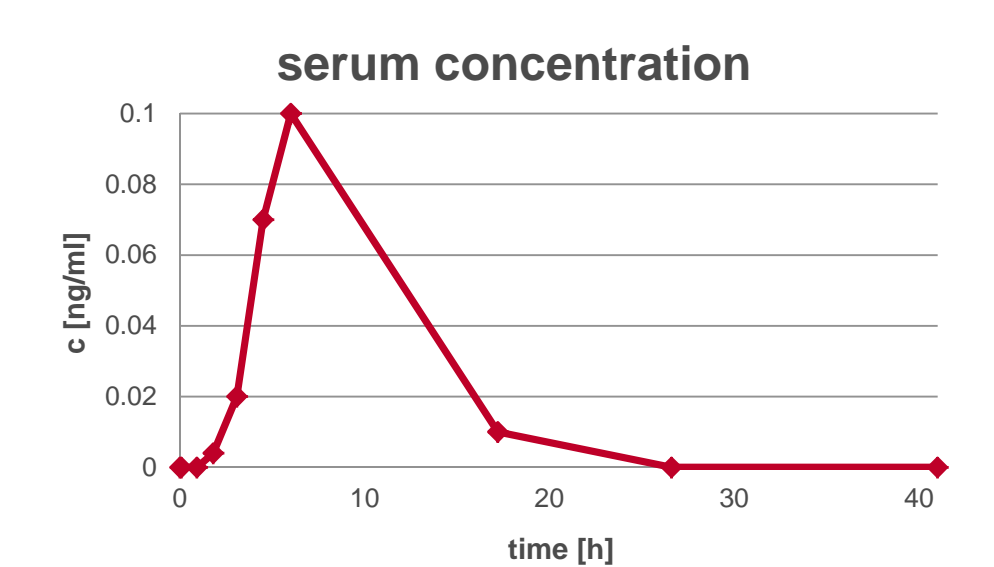


Fig.2: Serum concentration of cumyl-PINACA after 0.6 mg (oral)

Results

47 % of the e-liquids contained only nicotine as active ingredient. The other liquids contained one or more synthetic cannabinoids, e.g. 5F-APINACA, AB-PINACA or 5F-PB-22. Three of the liquids sold as 'c-liquids' (all from one retailer) contained 5F-cumyl-PINACA (Fig. 1).

To assess the relative potency of this new substance class – carrying a cumyl-moiety - a set of synthetic cannabinoids (AB-CHMINACA, AB-FUBINACA, AB-PINACA, AM-2201, cumyl-PINACA, EG-018, JWH-018, MDMB-CHMICA, THJ-2201) were characterised using the cAMP Biosensor Assay with CB1 as target (DiscoverX, Fremont, USA). The results of the Biosensor Assay are listed in Table 1.

Compound Name	Assay Format	EC50 (nM)	Curve Top	Max Response
AB-CHMINACA	Agonist	0.28	94.8	94.827
AB-FUBINACA	Agonist	0.89	97.4	97.82
AB-PINACA	Agonist	1.74	92.3	95.254
AM-2201	Agonist	0.45	103	101.41
Cumyl-PINACA	Agonist	0.06	93.7	92.86
EG-018	Agonist	40.7	74.3	71.826
JWH-018	Agonist	1.13	97.6	97.392
MDMB-CHMICA	Agonist	0.14	94.8	94.57
THJ-2201	Agonist	1.68	95.6	91.92

Table.1: results of the cAMP Biosensor Assay

Conclusion

The increasing popularity of e-liquids particularly among young people and the extreme potency of the added synthetic cannabinoids pose a serious threat to public health. There is a high risk of unintended poisoning, and in the long term prevalence of these drugs could rise in the younger population due to introduction of trendy products.

Main metabolites of cumyl-PINACA

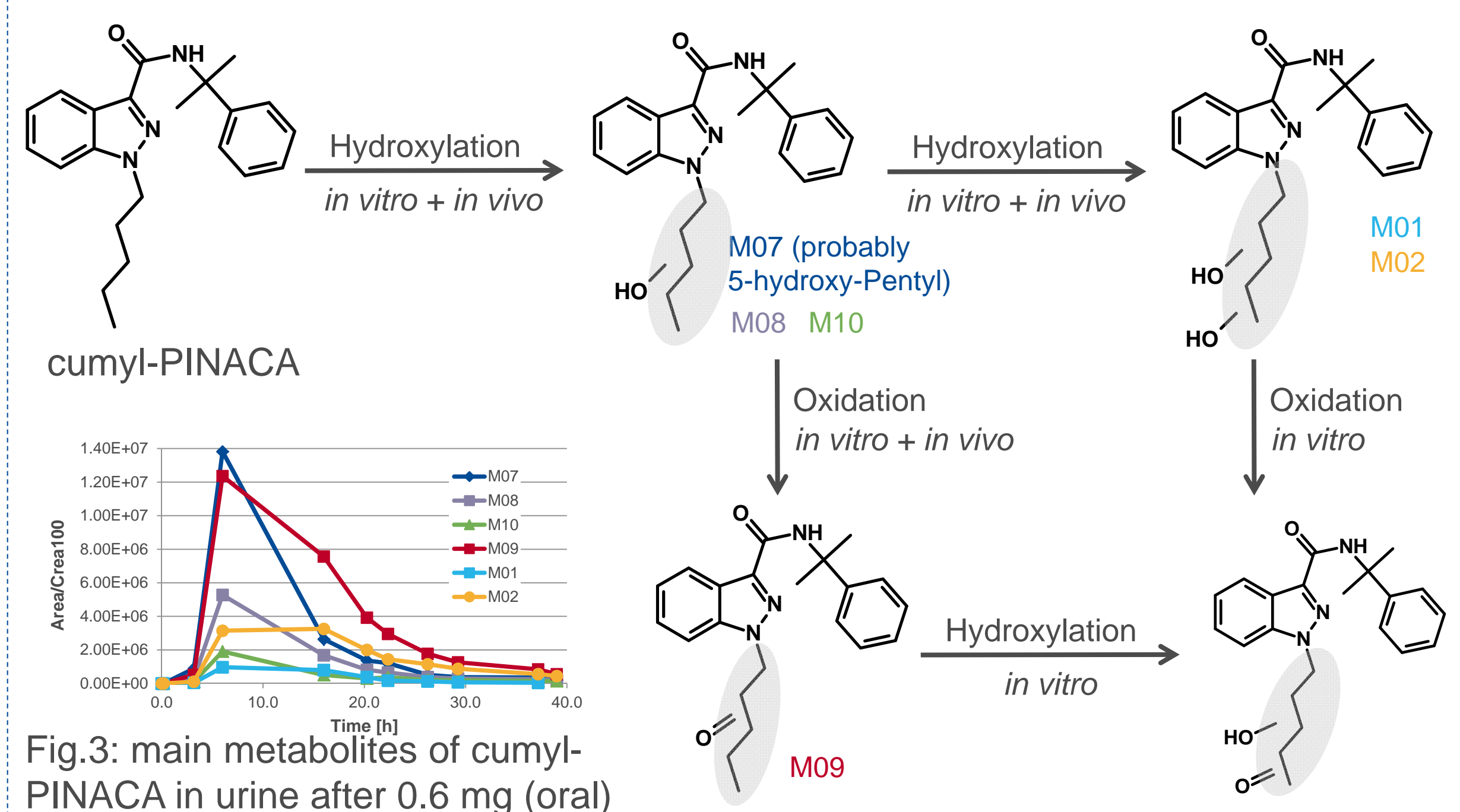
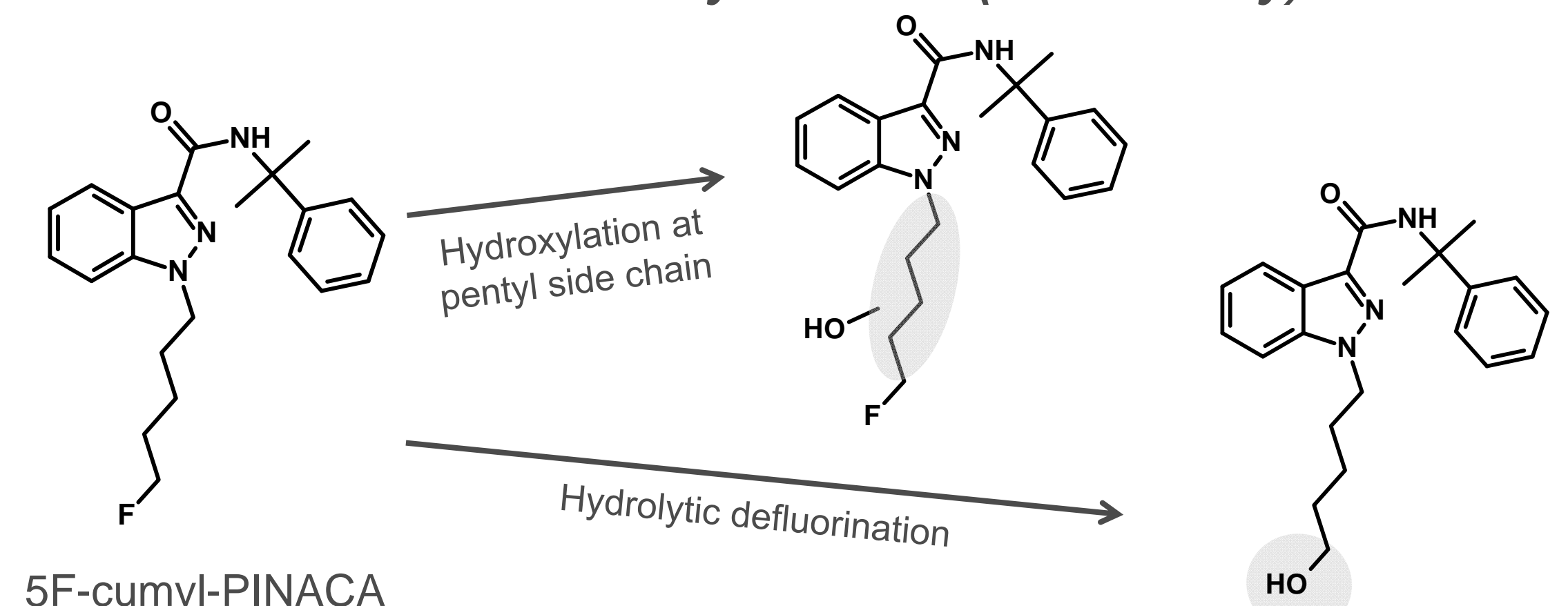


Fig.3: main metabolites of cumyl-PINACA in urine after 0.6 mg (oral)


Main metabolites of 5F-cumyl-PINACA (in vitro only)



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References:

[1] Camenga DR, Cavallo DA, Kong G, et al. Adolescents' and young adults' perceptions of electronic cigarettes for smoking cessation: A focus group study. Nicotine & tobacco research: official journal of the Society for Research on Nicotine and Tobacco 2015.

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