The volatilomic signatures of AGS, SNU-1, CLS-145 and HGC-27 gastric cancer cell lines

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Introduction

Despite the global decline in the incidence of stomach cancer, the disease is still extremely common leading to ~ 800,000 deaths/year worldwide. In fact, it is the third most common occurring cancer with a 5-year survival rate of less than 30%. Gastric cancer is also the second most frequent cause of cancer-associated deaths worldwide because of it being highly aggressive and promoting distant metastasis (typical metastatic sites are the lungs, liver and bones). The main reason for the low survival rate is late detection of the disease in symptomatic stages. Volatile biomarkers in the breath have the potential of use in detecting gastric cancers in its early stages. To gain knowledge on the origins of such biomarkers, we have undertaken *in vitro* studies of the volatilomic signature of gastric cancer cells, the results of which are presented here.

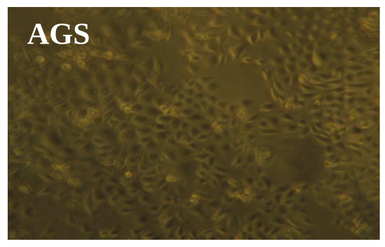
Methods

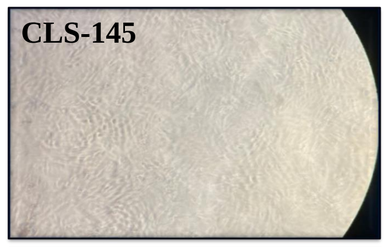
1. Cell lines cultivation under identical conditions

2. Pre-concentration method: headspace needle trap extraction (HS-NTE)

3. Analysis of VOCs using gas chromatography with mass spectrometry (GC-MS)

Cell lines





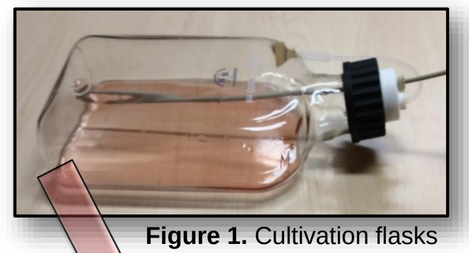
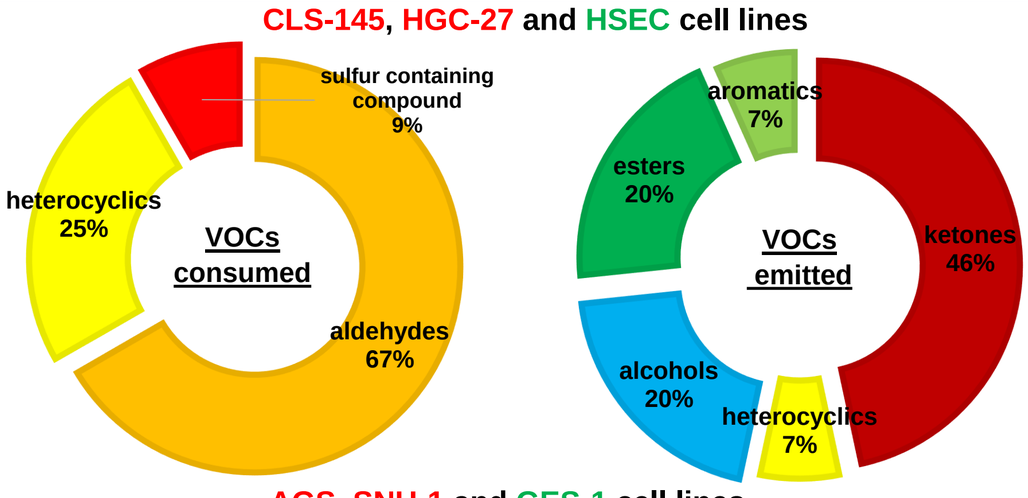


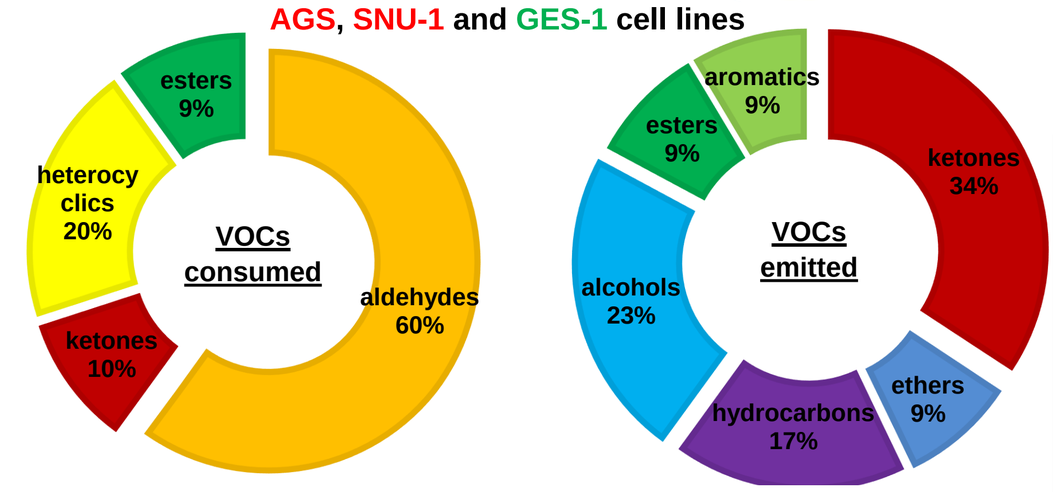
Figure 1. Cultivation flasks

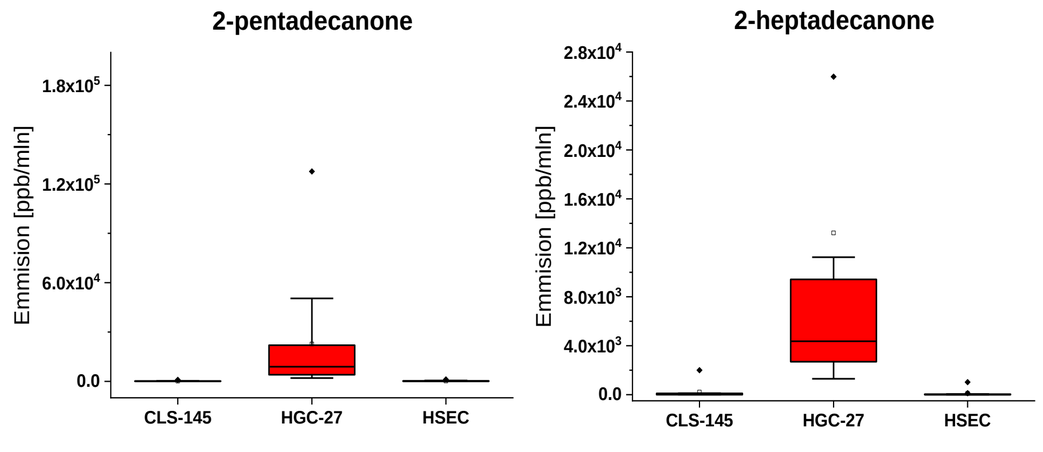
Results

CLS-145, HGC-27 and HSEC cell lines



AGS, SNU-1 and GES-1 cell lines





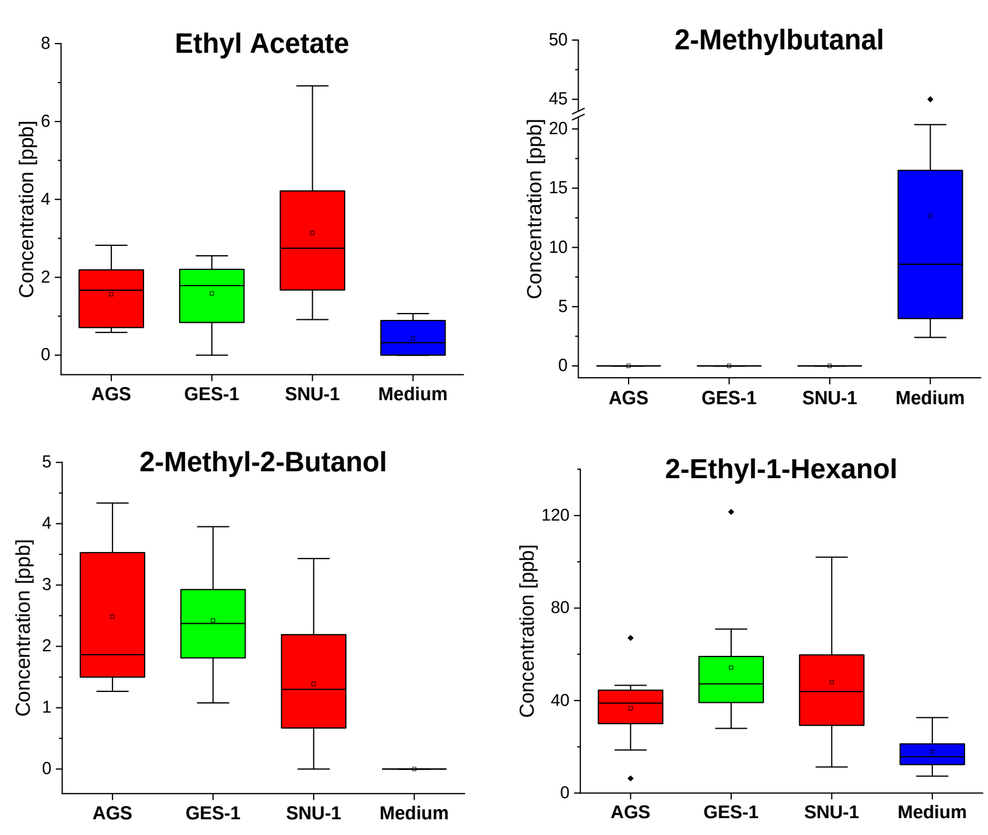
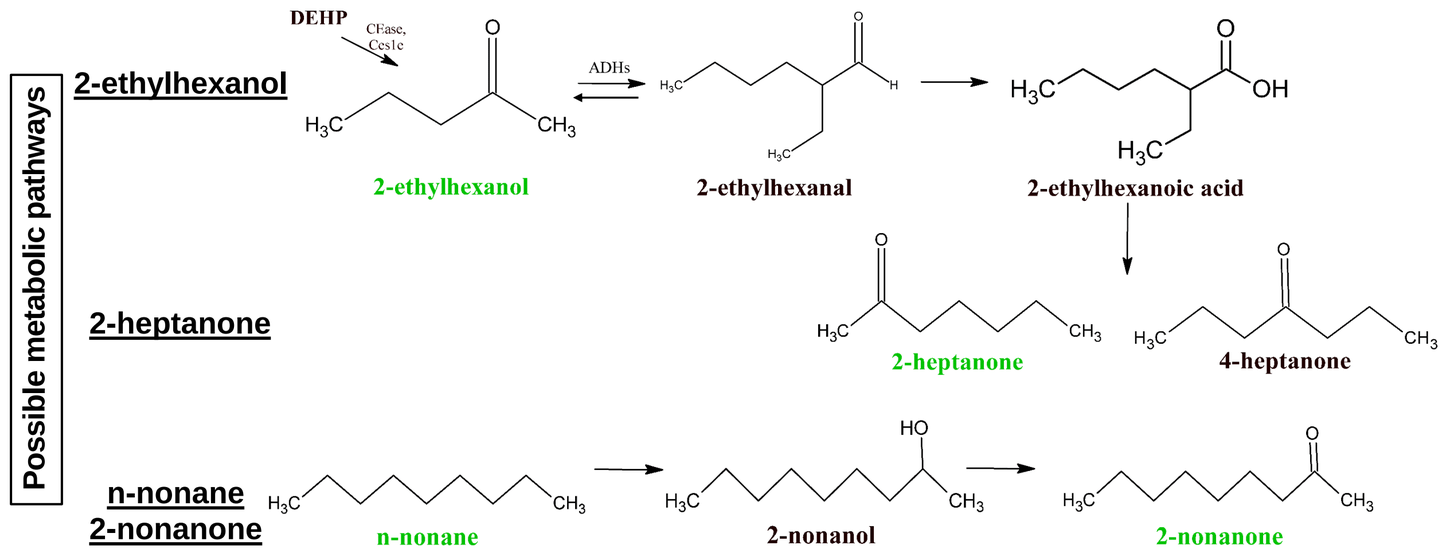


Figure 1. Concentrations [ppb] of 2-pentadecanone, 2-heptadecanone, ethyl acetate, 2-methylbutanal, 2-methyl-2-butanol and 2-ethyl-1-hexanol in the headspace of tested cell lines. The results were normalized to one million cells.

Table. 1. Summary of emitted VOCs by all cells under study (n.s.–not significant).

	VOC	CAS	CLS-145 vs HSEC p-value	HGC-27 vs HSEC p-value	CLS-145 vs HGC-27 p-value	AGS vs GES-1 p-value	SNU-1 vs GES-1 p-value	AGS vs SNU-1 p-value
RELEASE	2-Propanol, 2-methyl-	75-65-0	-	-	-	n.s.	n.s.	↑
	2-Butanone	78-93-3	-	-	-	n.s.	↓	↑
	Ethyl acetate	141-78-6	↓	↑	↓	n.s.	↑	↓
	Hexane, 3-methyl-	589-34-4	-	-	-	n.s.	↓	↑
	Benzene	71-43-2	-	-	-	n.s.	n.s.	↑
	1-Propanol, 2-methyl-	78-83-1	-	-	-	n.s.	↓	↑
	2-Butanol, 2-methyl-	75-85-4	-	-	-	n.s.	↓	↑
	2-Pentanone	107-87-9	n.s.	n.s.	n.s.	n.s.	↓	↑
	Ethyl propanoate	105-37-3	↓	n.s.	↓	↑	↑	↓
	3-Pentanone	96-22-0	-	-	-	↑	n.s.	↑
	Toluene	108-88-3	n.s.	n.s.	n.s.	-	-	-
	1-Butanol, 3-methyl-	123-51-3	↓	↓	↓	↓	↓	↓
	1-Butanol, 2-methyl-	137-32-6	↓	↓	↓	-	-	-
	Ethane, 1,1-diethoxy-	105-57-7	-	-	-	n.s.	↓	↑
	2-Pentanone, 4-methyl-	108-10-1	-	-	-	↓	↓	n.s.
	Ethyl 2-methylbutyrate	7452-79-1	n.s.	↑	n.s.	-	-	-
	2-Heptanone	105-42-0	↑	n.s.	n.s.	-	-	-
	Cyclohexanol	108-93-0	-	-	-	n.s.	↓	↑
	Cyclohexanone	108-94-1	-	-	-	n.s.	↓	↑
	2-Methyl-5-(methylthio)furan	2371-70-2	↑	n.s.	↑	-	-	-
	1-Hexanol, 2-ethyl-	104-76-7	↓	↑	↓	↓	n.s.	n.s.
	2-Nonanone	821-55-6	↑	n.s.	↑	-	-	-
	n-Dodecane	112-40-3	-	-	-	↓	n.s.	↓
	2-Undecanone	112-12-9	↑	n.s.	↑	n.s.	n.s.	n.s.
	2-Tridecanone	593-08-8	↑	n.s.	↑	↑	n.s.	↑
	n-Hexadecane	544-76-3	-	-	-	n.s.	↑	↓
	2-Pentadecanone	2345-28-0	↑	n.s.	↑	↑	n.s.	↑
	2-Heptadecanone	2922-51-2	↑	n.s.	↑	↑	n.s.	↑

Possible metabolic pathways



Conclusions

1. The results derived from this study provide evidence that gastric cancer modifies the volatilomic profiles of the cell lines;

2. Qualitative and quantitative differences in the cells volatilomic footprints are detected;

3. **HGC-27** and **AGS** cell lines are characterized by upregulated production of methyl ketones with an odd number of carbons;

4. **CLS-145** and **SNU-1** cell lines are marked by an increased production of esters and a downregulated production of alcohols;

5. Each of the gastric cancer cell lines has a distinct metabolic pattern.

Acknowledgement

This work has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no. 824986 and from National Science Centre (Poland) under grant agreement no. 2021/41/N/ST4/02307. DŚW acknowledges financial support through the project „AKCELERATOR ROZWOJU Uniwersytetu Jana Kochanowskiego w Kielcach" (Development Accelerator of the Jan Kochanowski University of Kielce), co-financed by the European Union under the European Social Fund, with no. POWR.03.05.00-00-Z212/18.