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Smoke Science / Product Technology
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Effect of sugar content on acetaldehyde yield in cigarette smoke

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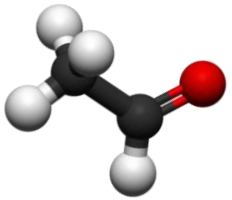
Acetaldehyde and cigarette smoke



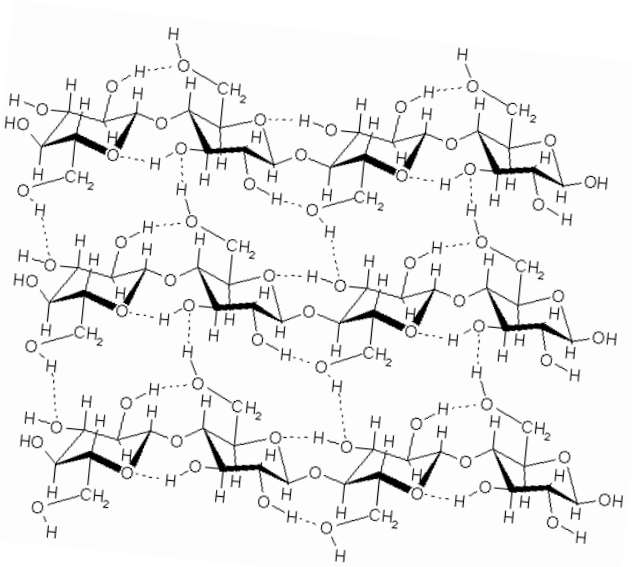
⇨Acetaldehyde in mainstream smoke is the major component in the vapour phase after oxygen, nitrogen , water, carbon monoxide and carbon dioxide

- Acetaldehyde has been classified in isolation as an animal carcinogen[1], and may be cytotoxic[2] or genotoxic[2]
- Acetaldehyde has been suggested to play a role in human smoking behavior[3]
  - Interaction with nicotine in the central nervous system
  - Formation of secondary condensation products which inhibit monoamine oxidase (MAO).

1- IARC 1999; 2-WHO 2001; 3-SCENIHR 2010

Acetaldehyde and cigarette smoke

A variety of studies suggest that acetaldehyde is generated in the mainstream tobacco smoke mainly from the pyrolysis (and oxidative pyrolysis) of **polysaccharides**, including cellulose, that are present in tobacco blend.



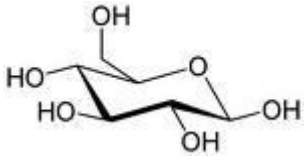
☞ Some scientific papers suggest that mainstream smoke acetaldehyde yields are related to soluble sugar levels quantified in the tobacco blends of different series of cigarettes

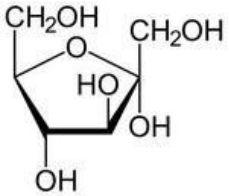
Soluble sugars and tobacco

Soluble sugars are natural components of tobacco. They are formed via enzymatic hydrolysis of starch during curing.

Monosaccharides (reducing sugars)

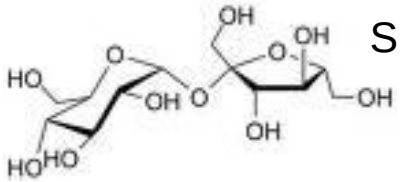
Glucose





Fructose

disaccharides

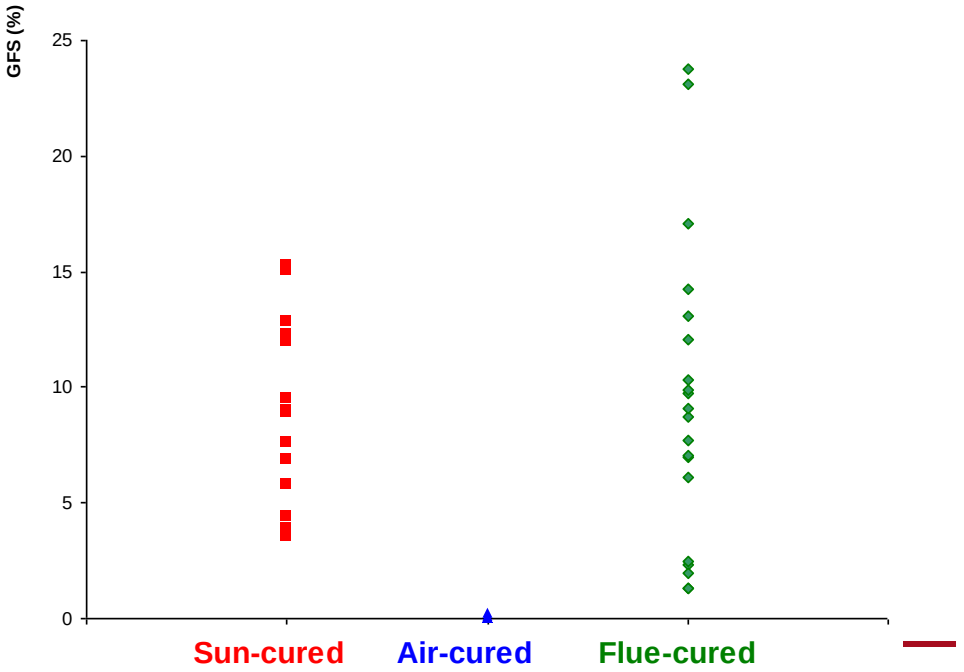


Sucrose

The sugar content in tobacco depends on curing type and is highly variable.

FC > SC >> AC

Sugars are largely metabolized during air-curing



Acetaldehyde and cigarette smoke

Soluble sugars are added to the tobacco blend in the form of casings, usually to those leaf components that have reduced sugar concentrations due to losses occurring during curing of, for example, air-cured Burley tobacco.

The contribution of tobacco ingredients on the composition of cigarette smoke is important and an active area of research

What is the contribution of soluble sugars to the production of acetaldehyde in mainstream smoke ?

Relationship between soluble sugars and mainstream smoke acetaldehyde yield?

D.F. Phillpotts, D. Spencer, D.T. Westcott. (1975) The effect of natural sugar content of tobacco upon the acetaldehyde concentration found in cigarette smoke. Beitr. Tabakforsch.; 8; 7-10

B.F. Zilkey et al. (1982) Chemical studies on Canadian tobacco and tobacco smoke. Tob. Int.; 184, 83-89

J.I. Seeman, M. Dixon, H-J Haussmann (2002) Acetaldehyde in mainstream tobacco smoke: Formation and occurrence in smoke and bioavailability in the smoker. Chem. Res. Toxicol. 15, 1331-1349

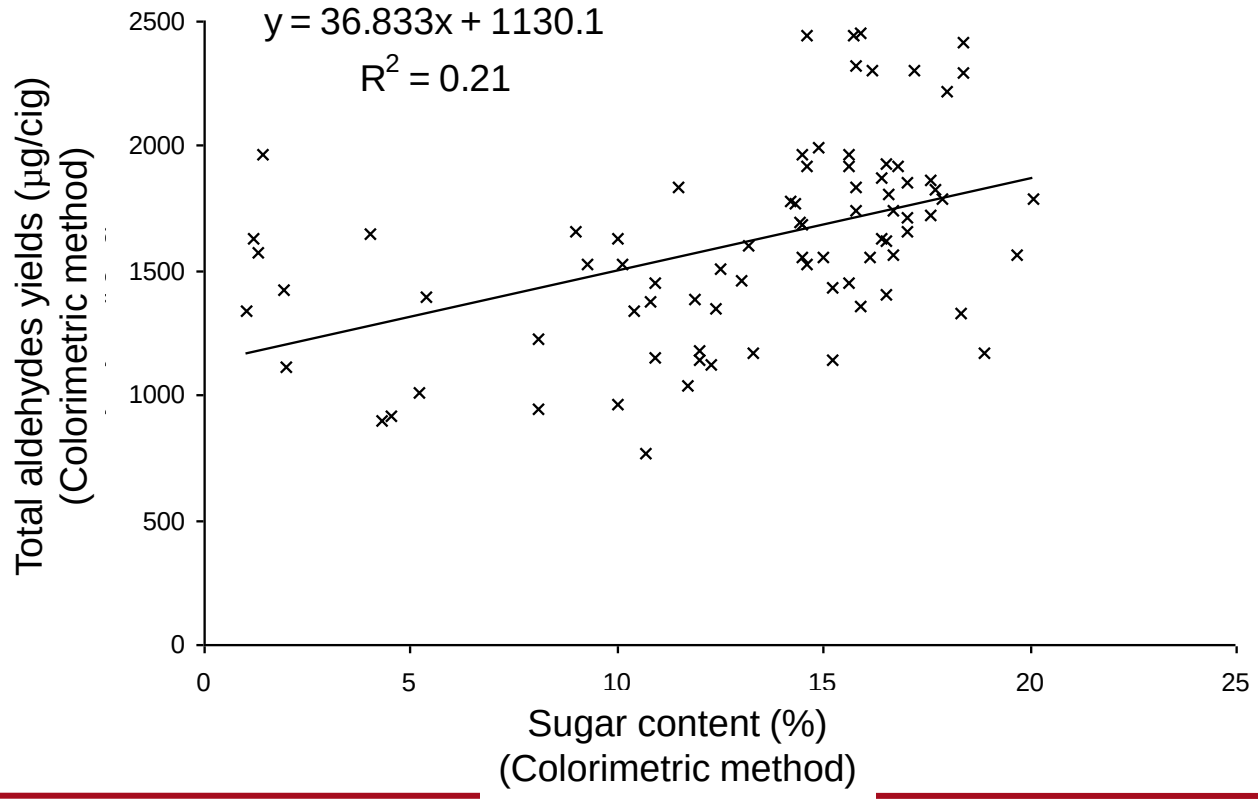
J. I. Seeman, S. W. Laffoon, A. J. Kassman (2003) Evaluation of relationships between mainstream smoke acetaldehyde and tar and carbon monoxide yields in tobacco blends of U.S. commercial cigarettes. Inhal. Toxicol. 15; 373-395

R. Talhout, A. Opperhuizen, J.G.C. van Amsterdam (2006) Sugars as tobacco ingredient: Effects on mainstream smoke composition. Food Chem. Toxicol. 44, 1789-1798

R.J. O'Connor, P.J. Hurley (2008) Existing technologies to reduce specific toxicant emissions in cigarette smoke. Tobacco Control 18; 139-148

Sugar/Acetaldehyde

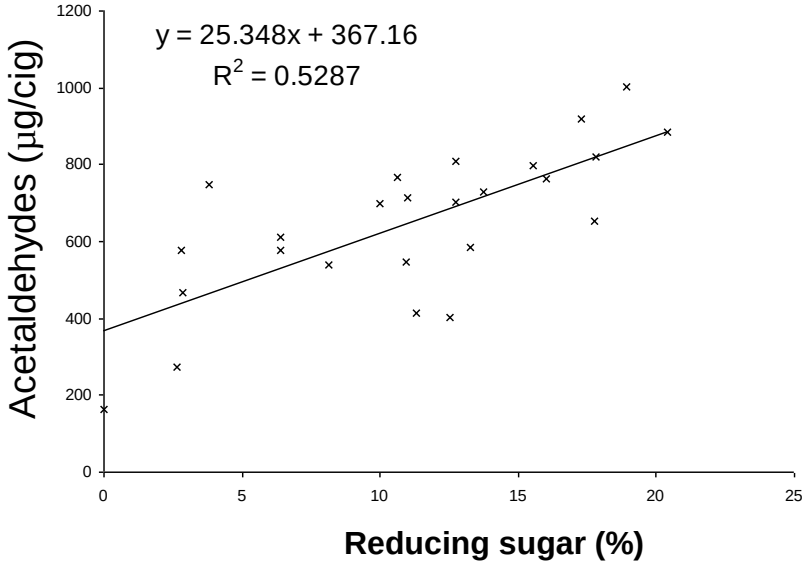
- 1975: Phillpotts et al. reported no correlation between MS aldehyde deliveries and sugar content of the tobacco (83 commercial brands)



D.F. Phillpotts, D. Spencer, D.T. Westcott. (1975) The effect of natural sugar content of tobacco upon the acetaldehyde concentration found in cigarette smoke. Beitr. Tabakforsch.; 8; 7-10

Sugar/Acetaldehyde

- 1982: A study published (Zilkey et al.) on 25 different experimental cigarettes with different sugar levels concluded that there was a significant correlation between acetaldehyde and reducing sugars

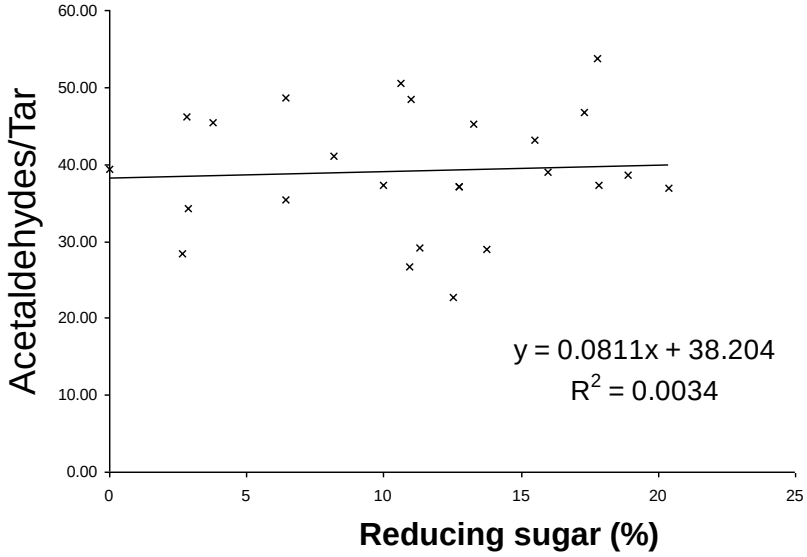


- 1982: Zilkey et al.

Cigarette tar yields ranged from **4.2 to 26.4 mg/cig**

Normalization of acetaldehyde yields by dividing by the tar yields

⇨No correlation between MS aldehydes deliveries/tar and sugar



B.F. Zilkey et al. (1982) Chemical studies on Canadian tobacco and tobacco smoke. Tob. Int.; 184, 83-89

Sugar/Acetaldehyde

- 2003: A benchmark study (Seeman et al.) on a large number of US cigarettes (*for the available data over the time period 1985-1993*) showed that the level of reducing sugars in the tobacco was not correlated to the level of acetaldehyde in mainstream smoke

		Correlation (r^2) of reducing sugars with :	
Year	Number of brands	Acetaldehyde	Acetaldehyde/tar
1985	135	0.0899	0.0000
1986	142	0.0715	0.0000
1987	185	0.0872	0.0004
1988	176	0.2349	0.0074
1989	4	*ND*	*ND*
1990	116	0.1633	0.0206
1991	264	0.1387	0.0004
1992	420	0.0847	0.0541
1993	102	0.0436	0.0209

ND: Non Determined due to small size of sample

J. I. Seeman, S. W. Laffoon, A. J. Kassman (2003) Evaluation of relationships between mainstream smoke acetaldehyde and tar and carbon monoxide yields in tobacco blends of U.S. commercial cigarettes. Inhal. Toxicol. 15; 373-395

Sugar/Acetaldehyde

- 2008: O'Connor and Hurley claimed that normalizing for tar may obscure a sugar-aldehyde relationship.
- The authors suggested applying a multivariate analysis to determine the relationship between smoke aldehydes and tobacco sugar taking into account the tar yields.

R.J. O'Connor, P.J. Hurley (2008) Existing technologies to reduce specific toxicant emissions in cigarette smoke. Tobacco Control 18; 139-148

Multivariate analysis

O'Connor and Hurley methodology (Phillpott's data):

Tob Control *2008;**17:**i39-i48 doi:10.1136/tc.2007.023689* ***Supplement***

Existing technologies to reduce specific toxicant emissions in cigarette smoke

R J O'Connor, P J Hurley

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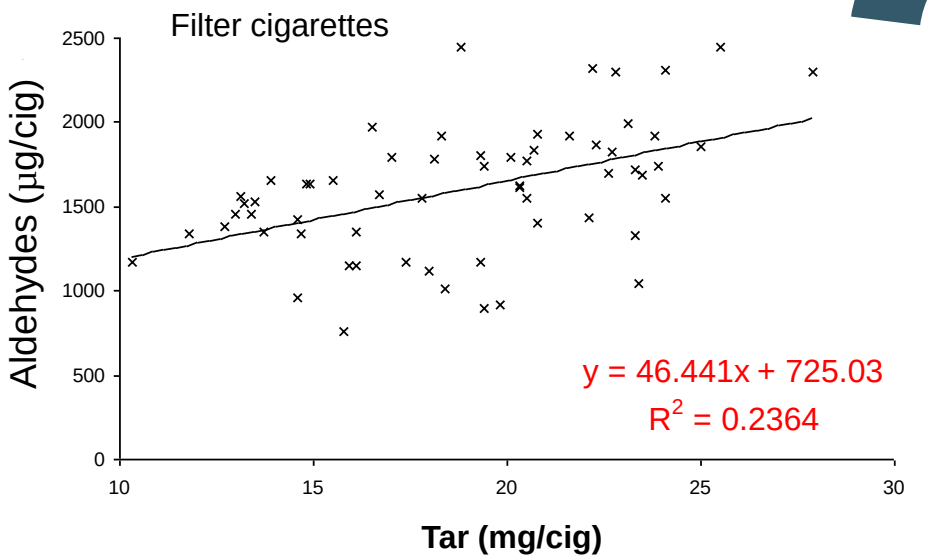
"…Zilkey et al[25] examined cigarettes prepared from tobacco types differing in sugar levels (that is, no added sugars). They reported that sugar levels accounted for over 50% of the variance in smoke acetaldehyde levels. Phillpotts of BAT reported that for 40 commercial UK brands, sugar content and moisture were unrelated to acetaldehyde yield, though acetaldehyde was related to TPM yield.[24] Similar associations were reported for brands from continental Europe. Re-analysis of the pooled data suggests that, if analysis is limited to filtered brands only, sugar content accounts for 23% of variability in aldehyde levels (β=0.48, p<0.001) and that sugar content is related to overall tar level (β=0.37, p<0.003). Published industry reports have generally normalised acetaldehyde yields to tar or TPM-these studies report no correlation between tobacco sugar content and smoke yields of acetaldehyde (reviewed by Seeman et al[18]). When we adjust the Phillpotts data for tar, we also find no relation. However, if one treats the problem multivariately, one sees a different pattern. If TPM is forced into the model first, it accounts for 23% of variance in aldehyde yield (β=0.48, p<0.001). This makes sense given TPM for filter cigarettes would be a surrogate for design features such as ventilation as well as mass of tobacco (which was not reported). If one then adds sugar content to the model, it is a significant predictor (β=0.35, p<0.004) and accounts for an additional 11% of variance in aldehydes and does not render TPM non-significant (β=0.35, p<0.004) by virtue of shared variance. So, normalising for tar may obscure a sugar-aldehyde association…."

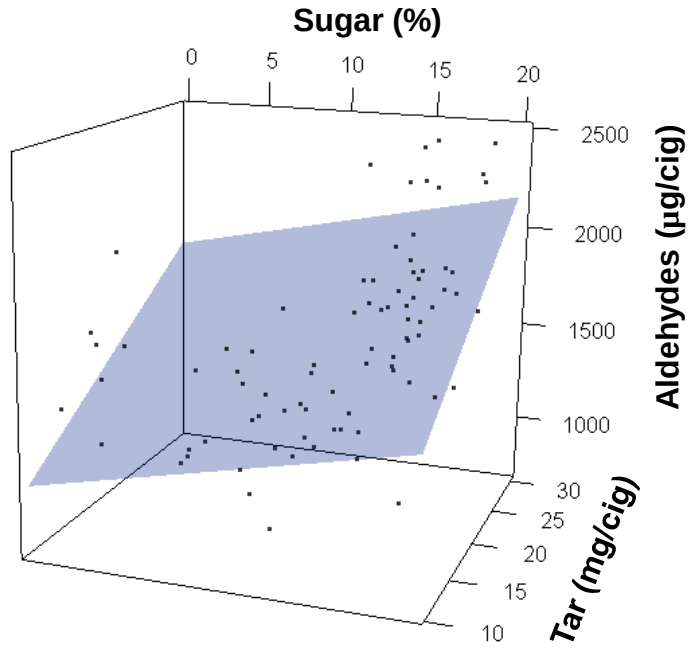
Multivariate analysis

O'Connor and Hurley methodology (Phillpott's data):

Aldehyde = α + β.Tar



Aldehyde = α + β1. Tar + β2. Sugar



Tar accounts for 23% of the variance in aldehyde yields

Multivariate correlation: 34%

O'Connor concluded "Sugar content is a significant predictor and accounts for **11%**"

Multivariate analysis

Multivariate analysis is based on the statistical principle of multivariate statistics, which involves observation and analysis of more than one statistical varaible at a time. In design and analysis, the technique is used to perform trade studies across multiple dimensions while taking into account the effects of all variables on the responses of interest.

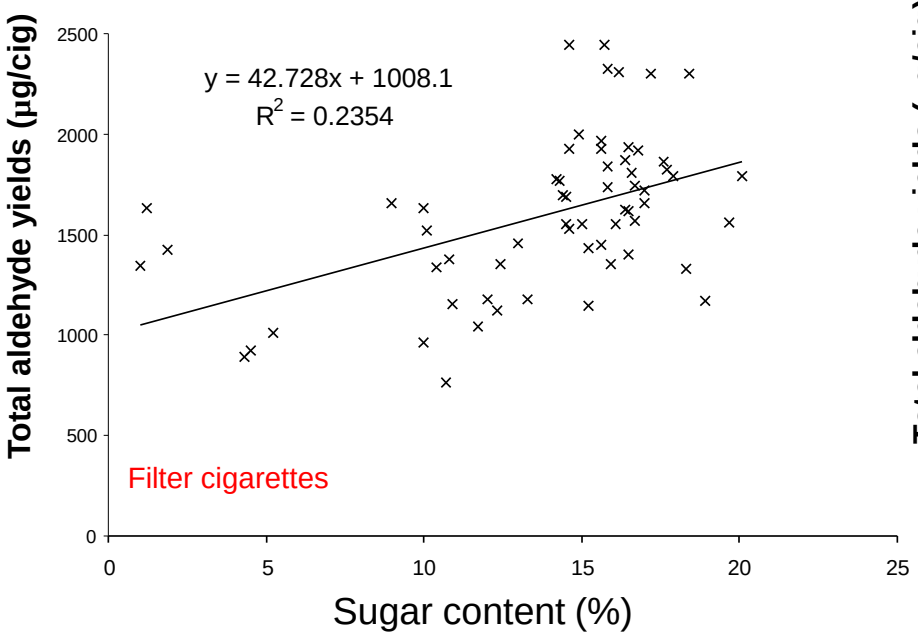
Multivariate analysis must take into consideration all the known factor in order to avoid misleading conclusion

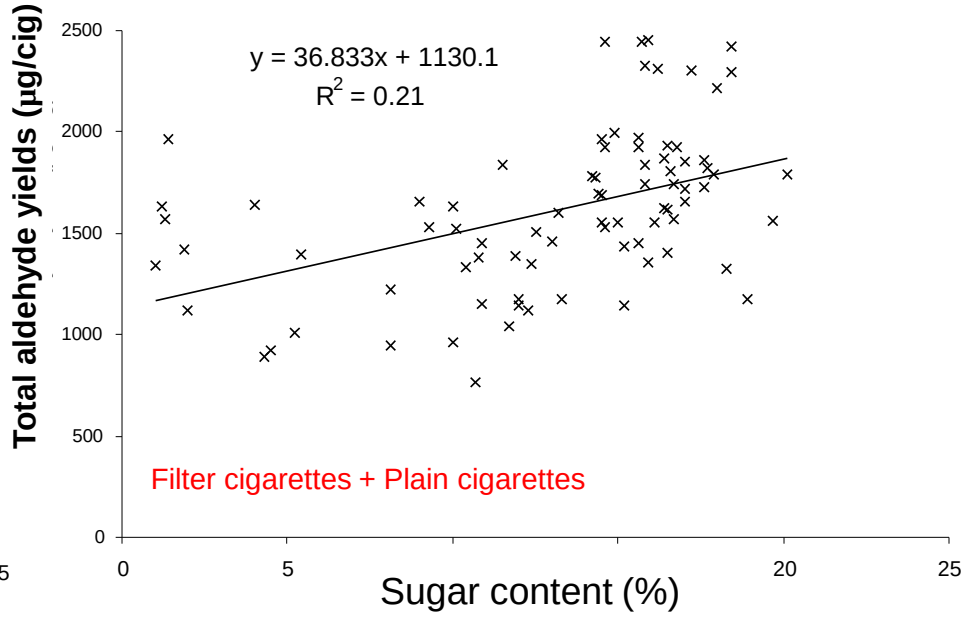
Simple linear regression : **Aldehyde = α + β.Sugar** or **Aldehyde/tar = α + β.Sugar**

Multiple regression : **Aldehyde = α + β1.Sugar + β2.Tar + …**

Multivariate analysis

- Re-analysis carried out by O'Connor **(Phillpott's data)** is limited to filtered brands only





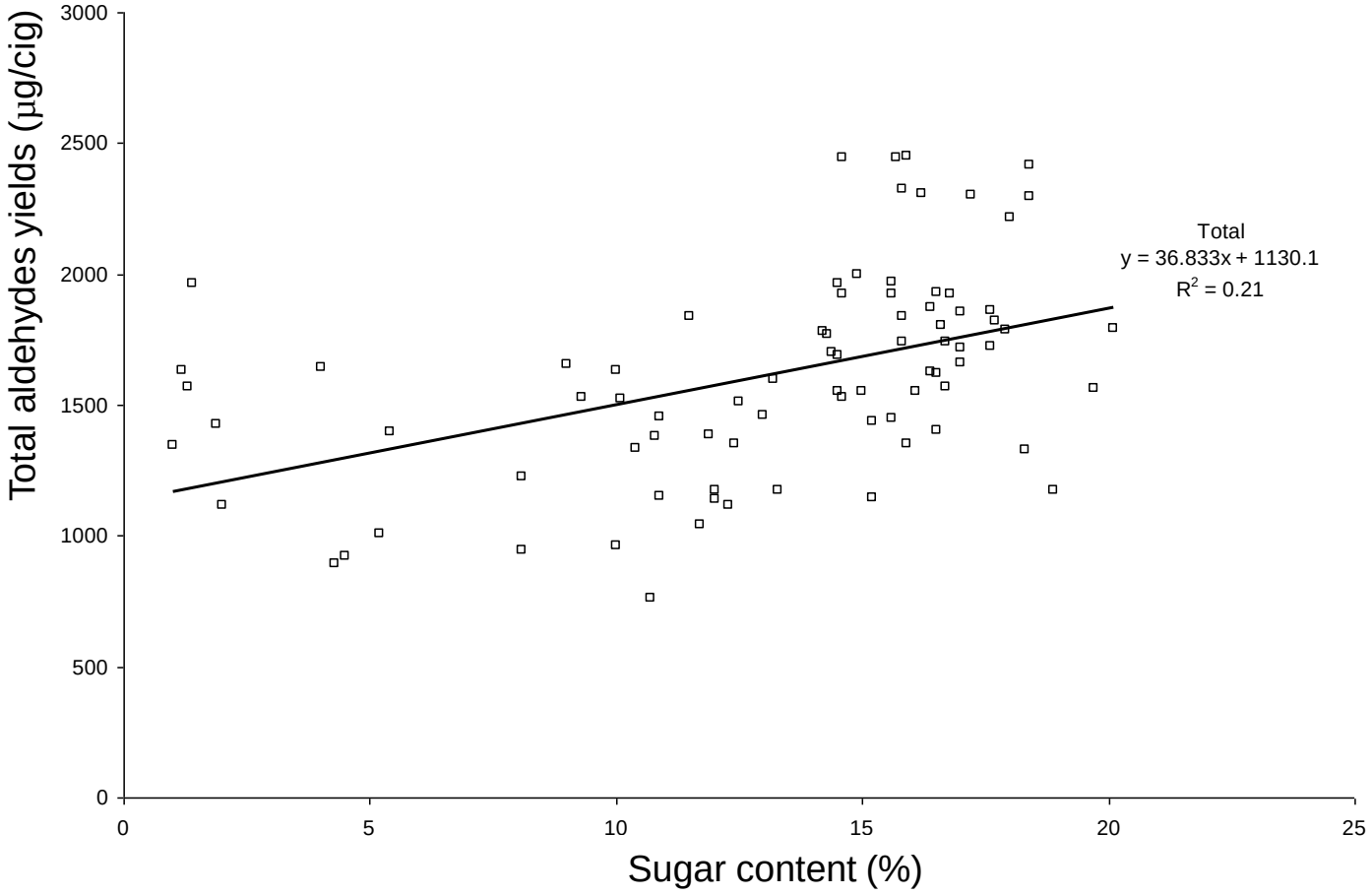
To be complete: a qualitative factor with two modalities (filter or plain cigarettes) can be added to the model.

D.F. Phillpotts, D. Spencer, D.T. Westcott. (1975) The effect of natural sugar content of tobacco upon the acetaldehyde concentration found in cigarette smoke. Beitr. Tabakforsch.; 8; 7-10

Multivariate analysis

- Country effect?

  Phillpotts et al. : "*Italian brands had low sugar and low aldehyde yield whilst French brands had even lower sugar but higher aldehyde yield*".



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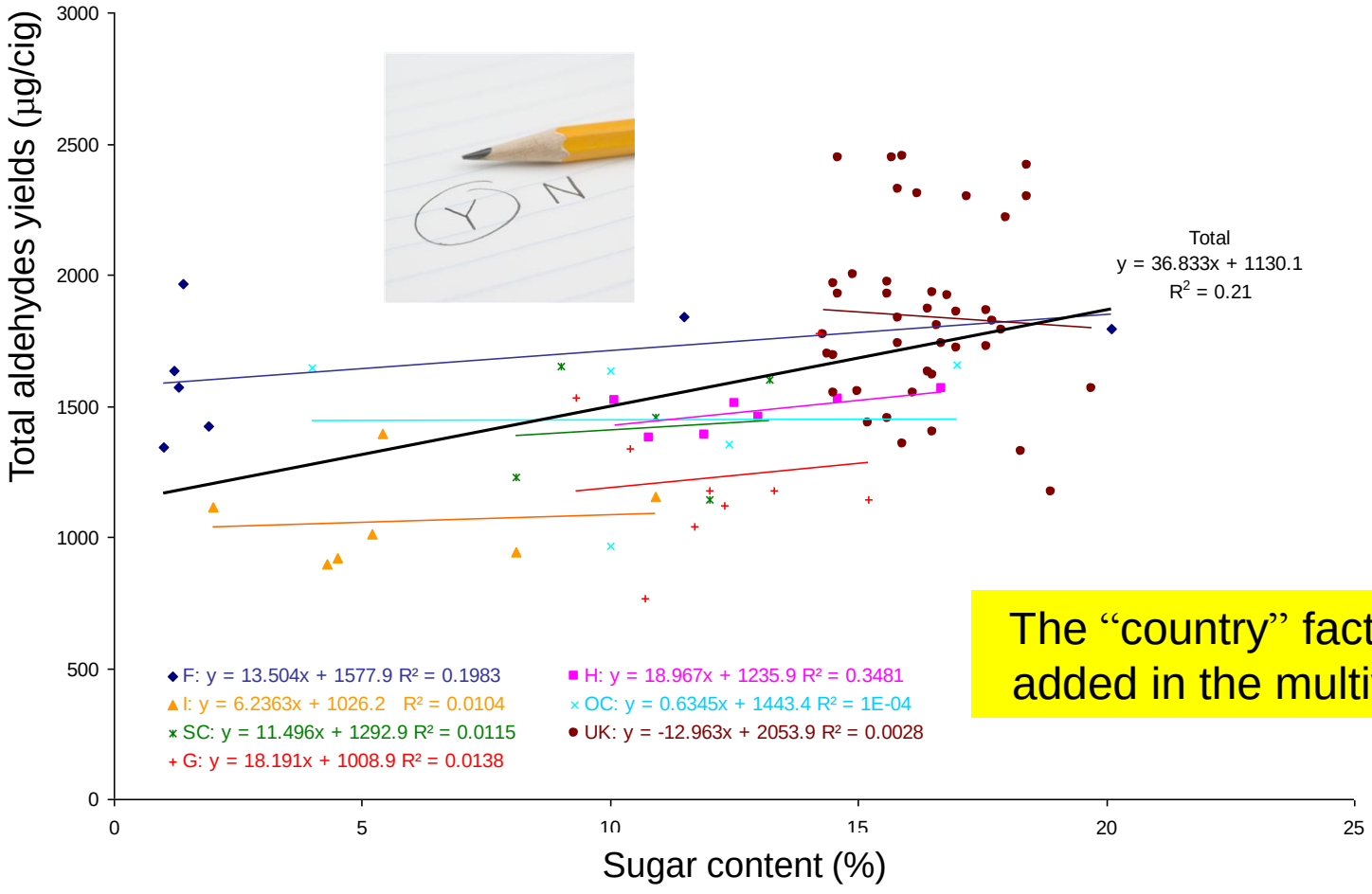


The "country" factor must also be added in the multivariate analysis

D.F. Phillpotts, D. Spencer, D.T. Westcott. (1975) The effect of natural sugar content of tobacco upon the acetaldehyde concentration found in cigarette smoke. Beitr. Tabakforsch.; 8; 7-10

Multivariate analysis*

Acetaldehyde = α + β 1.Filter or Plain + β2.Country + β3.Tar + β4.Sugar

Factors	Sum of Squares	DoF	Mean Squares	F ratio	P_value.	Significance
Filter or Plain	124805	1	124805	1.86	0.1772	NO
Country	2.86515E6	6	477525	7.11	0.0000	YES
Tar	876612.	1	876612	13.05	0.0006	YES
Sugar	5697.82	1	5697.82	0.08	0.7717	NO
Residue	4.83815E6	72	67196.5			
Total	1.23991E7	81				

DoF: Degree of Freedom

- No effect of Filter or Plain cigarette: 1 group
- No effect of sugar

Taking into consideration all these factors: sugar content **does not** have a significant impact on aldehyde yields

*General Linear Model (GLM)

Multivariate analysis*

To precisely evaluate the sugar effect per country a GLM analysis have been performed with the sugar factor nested in the country factor.

$$Acetaldehyde = \alpha + \beta 1.Country + \beta 2.Tar + \mathbf{\beta 3.Sugar(Country)}$$

Country	Sugar content effect	Tar level effect
UK	**NS**	**S**
France	**NS**	NS
Germany	**NS**	NS
Scandinavia	**NS**	NS
Italy	**NS**	NS
OC	**NS**	NS
Holland	**NS**	NS

OC: Other country (Belgium, Luxembourg, Switzerland); H: Holland

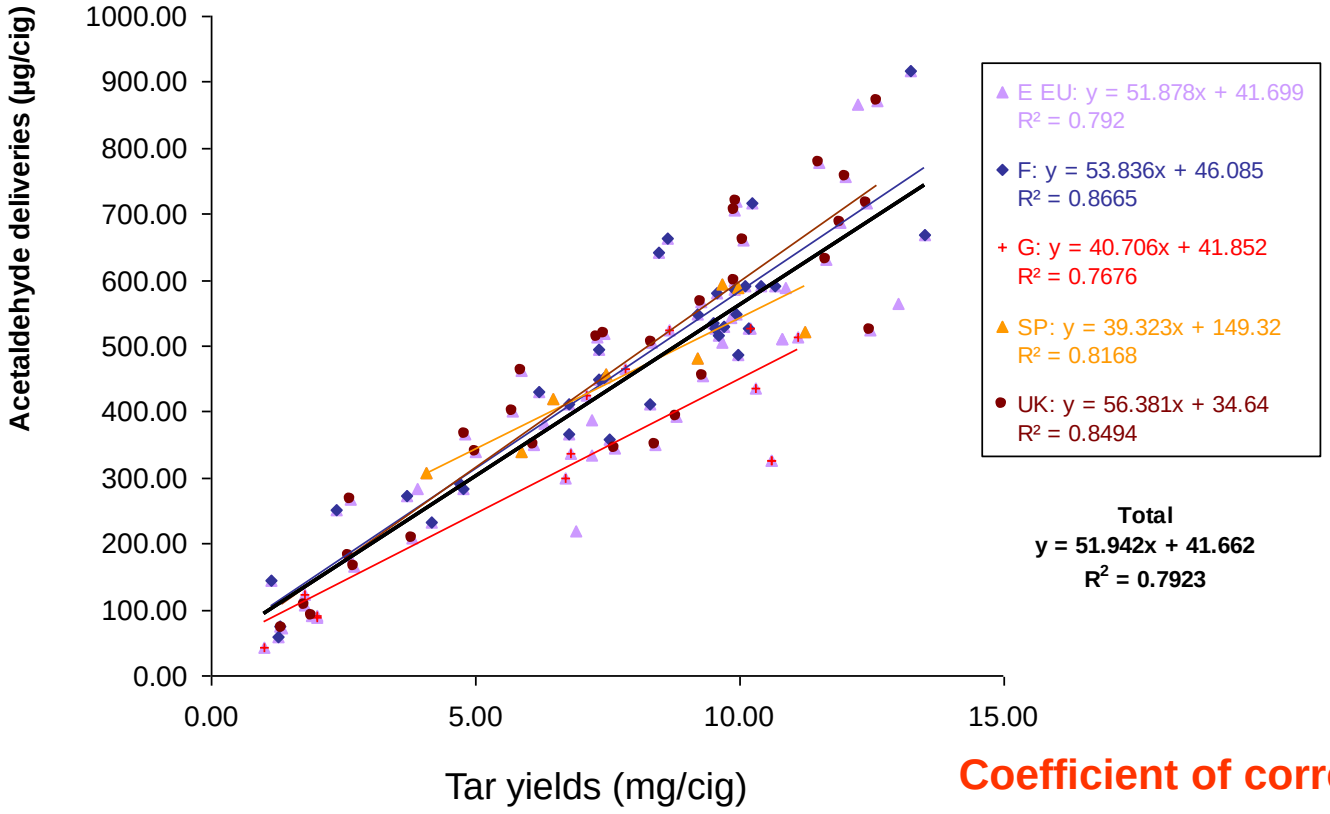
S: Significant
NS: Non-significant

No effect of sugar content on aldehyde yields whatever the country.

*General Linear Model (GLM)

Multivariate analysis
- Dataset of current products

Data set obtained in our laboratory on 99 commercial brands from EU market: 12 from East Europe (Poland, Hungary, Ukraine); 34 from France; 14 from Germany; 8 from Spain and 31 from UK.



Aldehydes measured by

DNPH – HPLC/UV method

Coefficient of correlation: 0.7923

UK: United Kingdom; F: France; G: West Germany; E EU: East Europe (Poland, Hungary, Ukraine); SP: Spain.

Multivariate analysis*

99 commercial brands from EU market:

- 9 Dark blended cigarettes
- 31 Flue-cured blended cigarettes
- 59 US blended cigarettes

$$Acetaldehyde = \alpha + \beta1.Blend + \beta2.Tar + \beta3.Sugar$$

Factors	Sum of Squares	DoF	Mean Squares	F ratio	P_value.	Significance
Blend	34020.4	2	17010.2	2.22	0.1139	NO
Tar	2.7989E6	1	2.79891E6	365.90	0.0000	YES
Sugar	7552.46	1	7552.46	0.99	0.3229	NO
Residue	719051	94	7649.48			
Total	3.6271E6	98				

DoF: Degree of Freedom

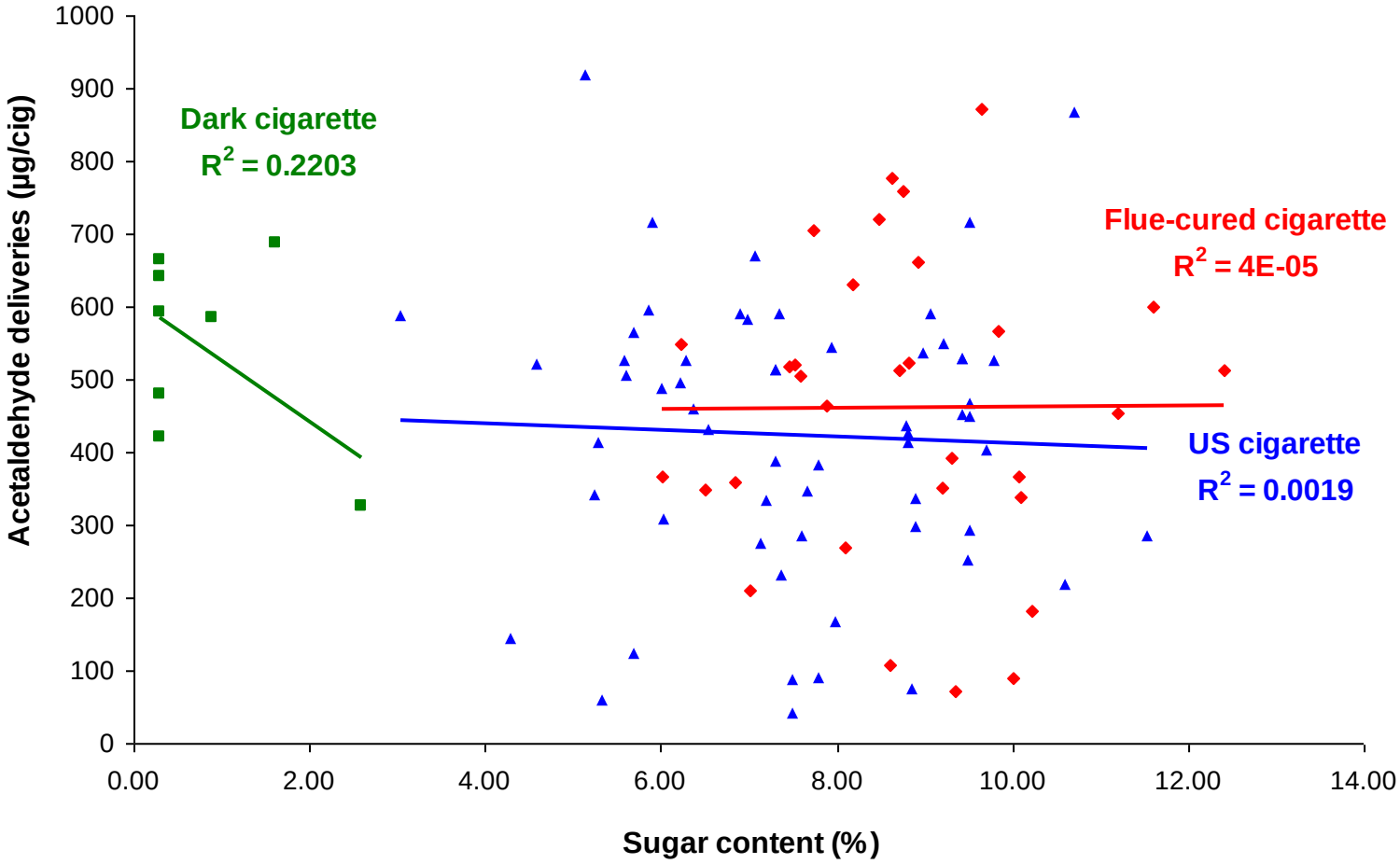
Sugar = GFS

Taking into consideration all the factors: sugar content does not have a significant impact on acetaldehyde yields

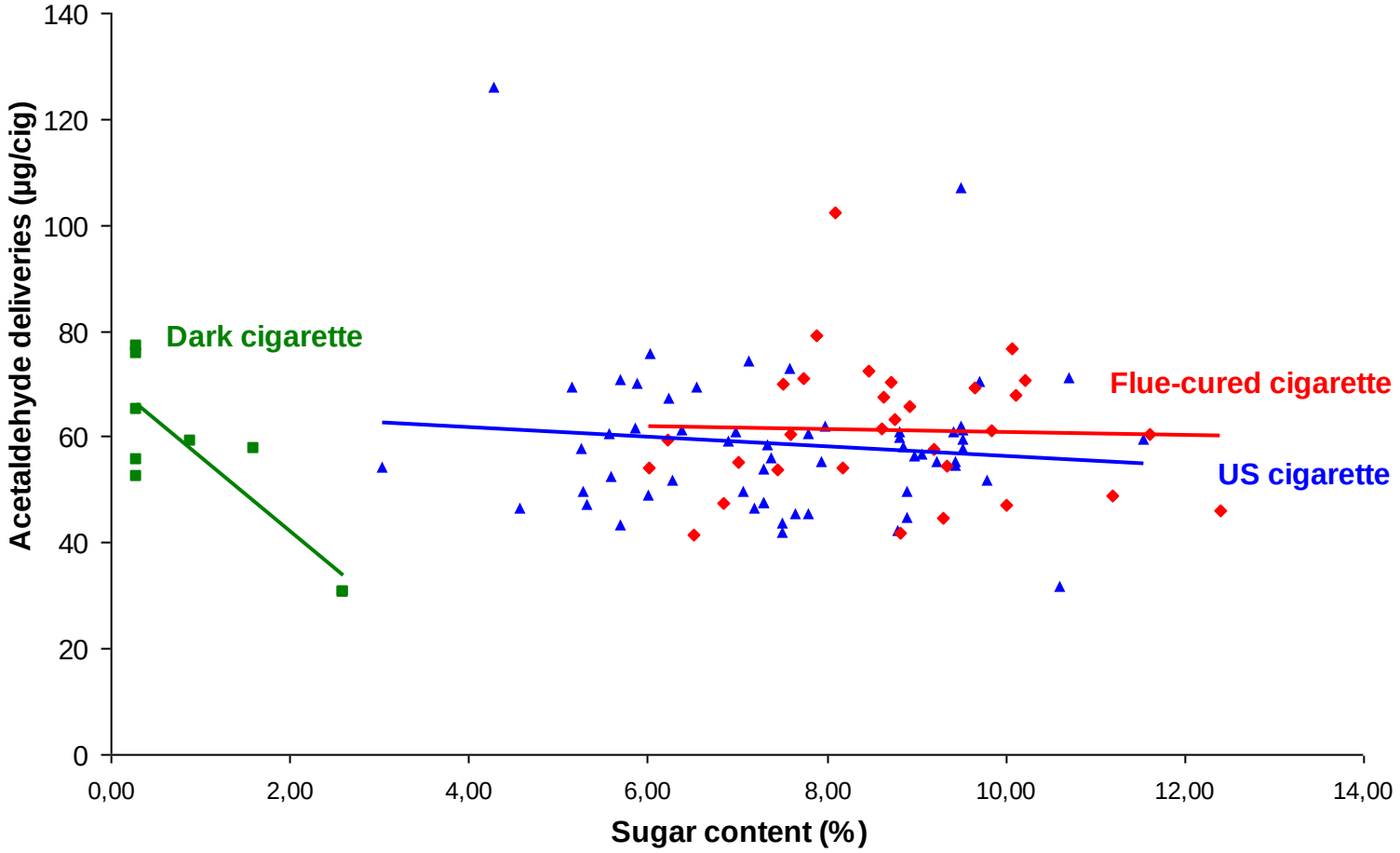
*General Linear Model (GLM)

Sugar measured as sum of sucrose, glucose and fructose by HPLC

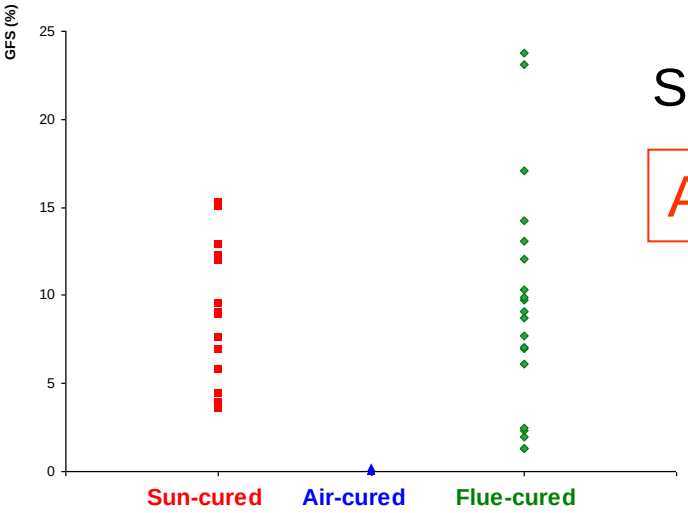
Acetaldehyde vs sugar content (Tobacco blend)



Acetaldehyde/tar vs sugar content (Tobacco blend)



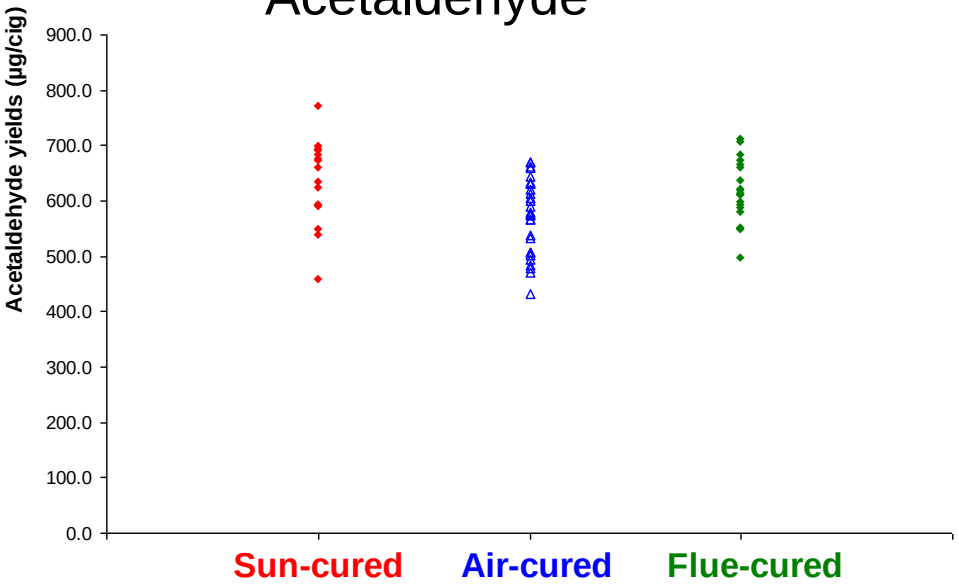
Leaf tobacco - cigarettes made from single grades (no added sugar)



Sugar content (%)

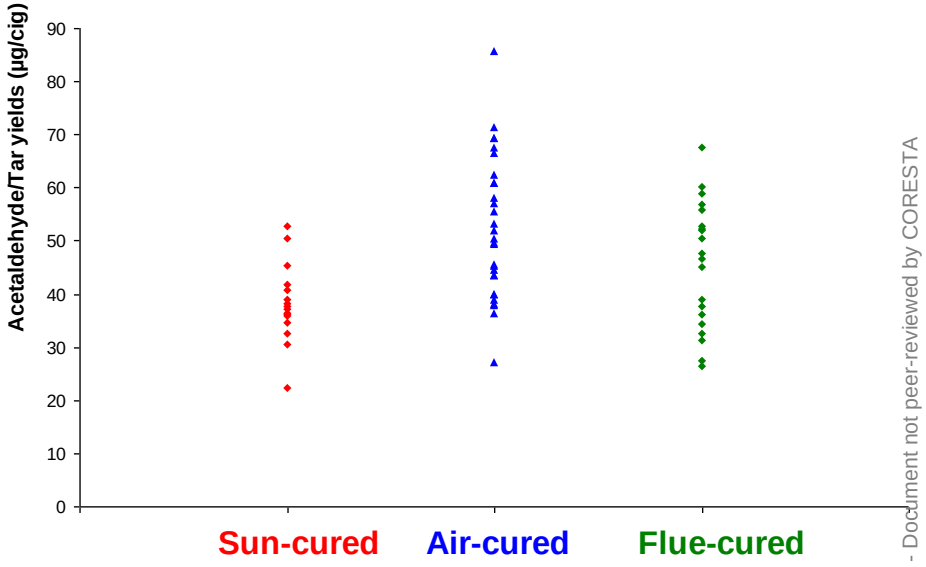
AC << FC = SC

Acetaldehyde



FC = SC = AC

Acetaldehyde/Tar



AC > SC = AC

Conclusion

- No relationship between soluble sugars and MS acetaldehyde yields has been proven even when using multivariate analysis
- Multivariate analysis must take into consideration all the known factor in order to avoid misleading conclusion
- No distinction of MS acetaldehyde yields between Flue-cured and US blended cigarettes irrespective of the sugar content
- No distinction of MS acetaldehyde between Flue-cured, Sun-cured and Air-cured tobacco (no sugar added)

Thank you !