The Oregon to Massachusetts Nicotine Connection The Pitfalls of Ignoring Simple Acid-Base Chemistry

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Outline of Presentation

- **Background**
  - Proposed Massachusetts DPH rules
  - Pankow's technique for unionized nicotine in TPM
- **Review of proposed technique**
  - Experimental
  - Calculations
- **Practical issues with proposed technique**
- **Theoretical issues with proposed technique**
- **Acids and bases in mainstream smoke**
- **Conclusions**

Background

- **In 2003, the Massachusetts Department of Public Health proposed additional regulations for cigarettes**
  - Proposed regulation (660.104) called for the reporting of unionized nicotine in smoke
  - Proposed regulation [660.200 (D)] specified technique described in article by J. F. Pankow of the Oregon Graduate Institute (*Chemical Research in Toxicology* 2003, 16, pp. 1014-1018)
- **Pankow's technique reportedly measures unionized nicotine in the mainstream particulate matter (PM, a/k/a TPM)**

Steps in Pankow's Technique (1)

1. **Smoke two cigarettes under Massachusetts vent-blocking and puffing conditions**
2. **Collect first 3 or remaining (about 8) puffs into separate Teflon bags**
3. **Wait about 15 minutes**
4. **Sample aerosol in bag and pass sample through particulate filter (0.5 µm pore size Zefluor PTFE Teflon membrane filter)**
5. **Effluent from particulate filter goes into Tenax-TA trap**

Steps in Pankow's Technique (2)

6. **Determine PM and nicotine on filter and nicotine on trap (c_p, c_{g1})**
7. **Add ammonia gas to the smoke aerosols in the bags**
8. **Resample aerosol in bag and pass sample through particulate filter**
9. **Effluent from particulate filter goes into Tenax-TA trap**
10. **Determine PM and nicotine on filter and nicotine on trap (c_p, c_{g2})**

Definitions Used in Pankow's Technique (1)

- **c_p = concentration of nicotine in PM filtered from aerosol sample**
  - Values should be similar to concentration of nicotine in TPM from Massachusetts smoking
- **$c_{g,1}$ = concentration of nicotine in gas stream after filtration of PM**
- **$c_{g,2}$ = concentration of nicotine in gas stream after filtration of PM with added ammonia**
- **α_{fb} = fraction of nicotine that is unionized**

Definitions Used in Proposed Technique (2)

- **$K_p = c_p/c_g$ = gas-particle partitioning coefficient for nicotine in smoke**
  - Assumes equilibrium for the partitioning of nicotine between the gas phase and particulate phase of the smoke aerosol
- **$K_{p,fb}$ = gas-particle partitioning coefficient for nicotine in smoke when there is no ionized nicotine present**
- **pK_a = 8.06 = disassociation constant for nicotine in water at 20° C**
- **pH_{eff} = calculated smoke pH**

Calculations Used in Pankow's Technique

- $(c_p/c_{g,2}) = K_{p,fb}$
- $(c_p/c_{g,1}) = K_p$
- $K_{p,fb}/K_p = (c_p/c_{g,2})/(c_p/c_{g,1}) = \alpha_{fb}$
- $pH_{eff} = pK_a + \log [\alpha_{fb}/(1 - \alpha_{fb})]$

Practical Issues with Pankow's Technique (1)

- **It does not provide the requested data**
  - Technique purports to provide concentration of unionized nicotine in PM
  - Technique does not give level of unionized nicotine in smoke
- **It is a research *technique*, NOT a *validated method***
  - Has not been validated for range of products
  - Has not been validated using equipment and conditions in cigarette testing laboratories

Practical Issues with Pankow's Technique (2)

- **There has not been an interlaboratory study to determine repeatability and reproducibility of the results**
  - Can the results be repeated at different times in the same laboratory?
  - Are the results reproducible from one laboratory to another?

Practical Issues with Pankow's Technique (3)

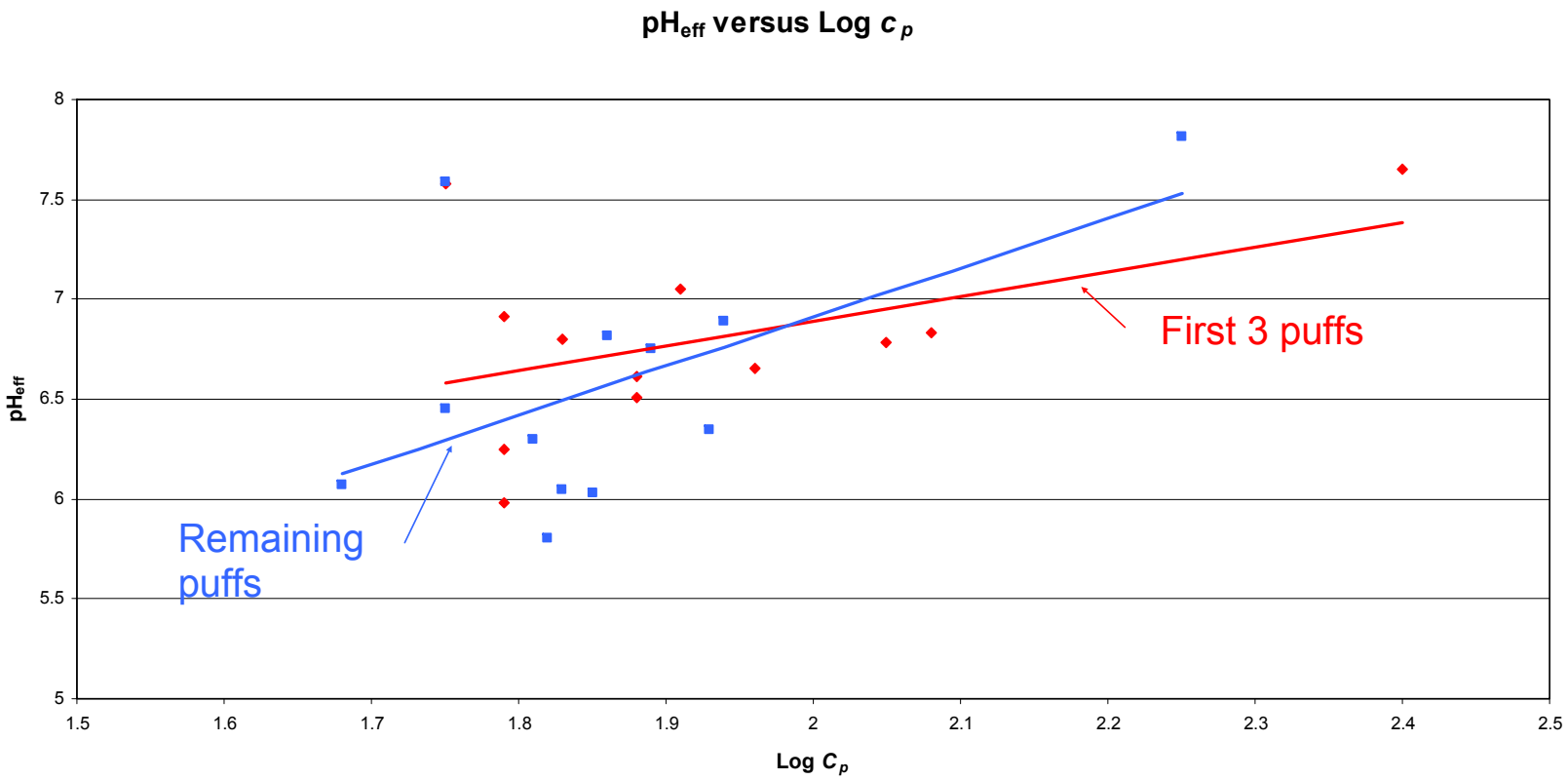
- **Non-standard conditions and equipment**
  - Cigarettes not conditioned prior to smoking
  - Cigarettes not smoked to standard butt length [the specified butt length (23 mm) would involve smoking into the tipping and filter for many products]
  - Equipment used for smoke generation and collection not proven (e.g., did Zefluor membrane retain all particulate matter?)

Practical Issues with Pankow's Technique (4)

- **Technique gives anomalous results**
  - Predominately flue-cured cigarettes known to give acidic smoke
  - Predominately burley or dark air-cured cigarettes known to give basic smoke
  - US blended cigarettes fall in between
  - GPC 100s, a blended product containing DAP gave much lower pH_{eff} than did American Spirit, a predominately flue-cured cigarette without additives

Theoretical Issues with Pankow's Technique (1)

- **pH_{eff} appears to be correlated with c_p, the concentration of nicotine in PM**
- **Is this a problem with the technique?**



Theoretical Issues with Pankow's Technique (2)

- **In addition to protonated nicotine, smoke contains numerous other acids and compounds that can react with ammonia**
  - Carbonic acid (from carbon dioxide and water produced from combustion of the tobacco)
  - Various organic acids
  - Numerous carbonyl compounds
- **Hold time (~15 minutes) between smoke collection and separation of particulate matter allows for reactions of ammonia**

Theoretical Issues with Pankow's Technique (3)

- **Major acids in mainstream cigarette smoke**
  - Protonated nicotine
  - Carbonic acid from reaction of carbon dioxide and water ($CO_2 + H_2O \leftrightarrow H_2CO_3$)
  - Total smoke water (gas-phase and particulate-phase) 2X to 10X amount of particulate-phase water
- **Is the amount of ammonia added by Pankow sufficient to neutralize acids?**

Acids and Bases in Mainstream Smoke (1)

	Virginia	Burley	Turkish	Blended
Puff count	15.5	10.5	18.1	8.4
"Tar" (μg/cig)	16430	12495	12670	11256
Nicotine (μg/cig)	2155	2153	833	941
TPM (μg/cig)	20150	15960	14480	13894
CO_2 (μg/cig)	50189	47397	51893	39698
NH_3 (μg/cig)	15.5	126	32.9	16.0

Data adapted from B. J. Ingebrethsen et al., *Aerosol Science & Technology* 2001, 35, pp. 874-886

Acids and Bases in Mainstream Smoke (2)

	Virginia	Burley	Turkish	Blended
Puff count	15.5	10.5	18.1	8.4
Nicotine (μmol/cig)	13.3	13.3	5.14	5.81
CO_2 (μmol/cig)	1141	1077	1179	902
NH_3 (μmol/cig)	0.912	7.41	1.94	0.944
Added NH3 (μmol/cig)	83.3	83.3	83.3	83.3

Data adapted from B. J. Ingebrethsen et al., *Aerosol Science & Technology* 2001, 35, pp. 874-886; and J. F. Pankow et al., *Chemical Research in Toxicology* 2003, 16, pp. 1014-1018

Conclusions on Pankow's Technique (1)

- **Insufficient ammonia added to neutralize smoke acids**
  - Invalidates underlying scientific basis for the technique
  - Adding more ammonia not satisfactory as amount needed to neutralize all acids would require detailed knowledge of each product's smoke chemistry
- **Hold time of ~ 15 minutes allows for chemical and physical changes to occur**

Conclusions on Pankow's Technique (2)

- **It should not serve as a basis for regulation**
  - Not scientifically valid
  - Not a method that has been validated through proper scientific study
- **It does not provide the level of unionized nicotine in smoke as specified in the proposed regulations**