



Interoffice Memorandum

Aug. 13

Please include
for 8/13 meeting
E. B. ...

Subject: The "Mitigant" Approach to
Modifying Biological Activity
of Tobacco Smoke

Date: July 20, 1992

To: Dr. W. M. Hildebolt

From: William S. Simmons

In one of his recent "get acquainted" sessions, Dr. Ehmann alluded to his interest in the potential for using "mitigants" to modify or alter the biological activity of tobacco smoke. As you are aware, several groups here at BGTC (including the Smoking and Health Division) have noted the presence in tobacco of several chemical families having properties that may render them useful as biological mitigants if they could be induced to transfer into mainstream during the smoking process. Virtually all of these chemical species share an important chemical trait - anti-oxidant potential. While the carotenoid family has received the most attention, it is by no means the only or even most promising naturally occurring tobacco constituent with mitigating potential.

Investigators at Hoffman-LaRoche (Conney and Newmark), Case Western (Dave Bickers) and the University of Minnesota (Lee Wattenberg) have published studies on the:

- > anti-oxidant potential
- > anti-mutagenic potential
- > anti-carcinogenic potential

of several members of the lignin/polyphenol family of compounds.

For instance, Conney and Newmark have shown that ellagic acid can dramatically block the mutagenic potential of B(a)P metabolites (1). These same investigators demonstrated that caffeic acid and ferulic acid block the formation of nitrosamines in vivo and concluded (2):

"The results of this study suggest that dietary caffeic acid and ferulic acid may play a role in the body's defense against carcinogenesis by inhibiting the formation of N-nitroso compounds".

Newmark (3) has authored a provocative review of the potential for dietary phenolics and pyrrole pigments as blockers of chemical carcinogenesis.

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A similar review by Ramel, Alekperov, Ames, Kada and Wattenberg (4) was prepared under the auspices of the International Commission for Protection Against Environmental Mutagens and Carcinogens (ICPEMC) in which the anti-carcinogenic potential of anti-mutagens was discussed.

Because of his stated interest in this subject, you may want to mention to Dr. Ehmann that while this approach has not been systematically pursued, it is under evaluation.

References

1. Wood, Hagan, Change, Newmark, Lohr, Yagi, Sayer, Jerima, and Connoy. Inhibition of the Mutagenicity of Bay-Region Diol Epoxides of Polycyclic Aromatic Hydrocarbon by Naturally Occurring Plant Phenols: Exceptional Activity of Ellagic Acid. *Proc. Nat. Acad. Sci.* (1982) 79:5513-5517.
2. Kuenzig, Chan, Norkas, Holowaschenke, Newmark, Mergens and Conney. Caffeic and Ferulic Acid as Blockers of Nitrosamine Formation. *Carcinogenesis* (1984) 5:309-313.
3. Newmark HL. A Hypothesis for Dietary Components as Blocking Agents of Chemical Carcinogenesis: Plant Phenolics and Pyrrole Pigments. *Nutrition and Cancer* (1984) 6:58-70.
4. Ramel, Alekperov, Ames, Kada and Wattenberg. Inhibitors of Mutagenesis and Their Relevance to Carcinogenesis. ICPEMC Publication No. 12. *Mutation Research* (1986) 168:47-65.



William S. Simmons