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BLOND TOBACCO AS A CARCINOGEN

By Professor Dr. Angel H. Ruffo

(1) In an earlier article in which I was concerned with investigations conducted to provide knowledge on the carcinogenic action of tobacco, I pointed out results which demonstrate that this action resides in combustion products.

(2) It is the tar contained in smoke, and not the nicotine, that acts upon the cancerization of the tissues, in the same form and following the same histopathogenic process that takes place with coal tar.

(3) Experimentation conducted on animals reproduces the clinical process observed in man, which has resulted in that, from a hypothetical trial indicating tobacco as a carcinogen. This has become a positive fact.

(4) Thus it is that the relationship existing between pulmonary bucolaryngeal cancer and tobacco acquires, in actuality, the value of an experimental finding.

(5) With regard to this, not only do we find the fact of intensive cancer development in male smokers, in the locations that come into contact with smoke, but also another fact, perhaps of even greater importance and upon which I must insist: this refers to an observation to which I have made reference on other occasions, to the differences that exist between the two sexes regarding these locations. (6) It is in the lips, the tongue, the pharynx, the larynx and the lungs where an accentuated disproportion is established for women.

(7) Taking into consideration the figures produced in the last 5 years, it is observed, in general, that cancer in all of these locations is found in men more than 90% of the time; while in women, especially for certain locations such as the larynx; its production is reduced, with years such as 1932 in which not a single female patient with cancer in this location was presented. (8) It is only in these past years that we have observed some cases in these locations, the total of which reaches 14, all of these women being heavy smokers. (9) These are the results with which our experiments have provided us, giving tobacco a considerable role in the development of cancer of the mouth, not only as a aetiological factor, but also so as to establish a prophylaxis in the social struggle against this evil.

(10) The above-mentioned experimentation (1) refers to the tar obtained from black Kentucky tobacco. (11) This refers to a product of distillation that occurs at between 120° and 350° C.; that presents itself with the characteristics of a conglomerate with resinous nature, a dull color, an alkaline reaction and having a strong and unpleasant odor.

(12) This product does not contain nicotine. (13) On the other hand, the bodies from which it is made up are numerous, containing: carbon monoxide, carbon dioxide, ammonia carbonate, acetic acid and acetates, citric acid, phenylic acid, succinic acid and succinates, fumaric acid, pyrrole and its derivatives,

(1) A.H. Roffo, "Tobacco As a Carcinogen" in the Boletín del Instituto de Med. Exp., No. 42, pg. 287.

3848+ Roffo AH: El tabaco rubio como cancerígeno. Bol Inst Med Exp 15: 5-22, 1938. [SOA 230; DTH Exhibit 62, 63 page 496; TOP 2048; Cited P81, P234]

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pyrrolidine and methylpyrrolidine, chlorophyll derivatives, resynthesized bodies, with stable benzene nuclei (hydrocarbons, phenanthrene, anthracene, benzopyrene).

(14) The experiments undertaken with this tar from black tobacco were conducted on rabbits, with daily applications on the inner surface of the ear.

(15) Tumors have been produced abundantly, in some 98% of the animals.

(16) The papillomatous lesions appear after 7 months of this treatment, acquiring, from 9 to 12 months after the beginning of the experiment the anatomical and histological characteristics of a carcinoma.

(17) Now, given the results and in complement to the previous experimentation, it remains to be determined whether blond tobaccos also produce a carcinogenic tar.

(18) This test was one which had to be undertaken, taking into account above all the immoderate use of blond tobacco in high social circles, where it is considered to be a distinctive and luxury tobacco, and generally thought to be more inoffensive than black tobacco.

(19) The experiment upon which this article is based was conducted with two types of blond tobacco, which are found in commercial listings as Egyptian and Turkish.

(20) The tar of these tobaccos is a product whose characteristics are similar to that of black tobacco; it forms a resinous conglomerate, with a strong and unpleasant odor which rapidly irritates the mucous membranes and is of an alkaline reaction.

(21) In the first place, the quantity of tar produced by these tobaccos in comparison with the black Kentucky tobacco was determined, leading to the discovery that the former is much greater, which was to be expected; and furthermore, from the time that these tobaccos are much more resinous, which can be seen in the following summary:

Tobacco	Quantity of tar per kilo
Kentucky	41 grams
Egyptian	68.6 grams
Turkish	72 grams

(22) In the second place, toxicity was determined. (23) For technical reasons, this was done with distilled water, which contained highly toxic hydrosoluble products, such as pyridine, methylpyrrolidine, ammonia bases, succinates, acetates, etc.

(24) It is interesting to point out that this product contains no nicotine.

(25) This toxicity is also more accentuated in these tobaccos, especially for the Egyptian tobacco; because if 5.33 c.c. are needed to kill one kilo of a rat with the Kentucky tobacco, 2.22 c.c. are sufficient to obtain the same result with Egyptian tobacco, as can be seen in the following summary:

Tobacco	Toxicity per kilo of animal (rat)
Kentucky	5.33 c.c.
Egyptian	2.22 c.c.
Turkish	3.00 c.c.

(26) Furthermore, there is a relationship between this toxicity and the fact that these tobaccos contain highly toxic products, such as pyridine.

(27) Thus, it is observed that if Kentucky tobacco has a toxicity of 5.33 c.c. with a pyridine content of 0.48; the Egyptian tobacco, which has a double toxicity, also has a double content of pyridine, which can be seen from the following summary:

Tobacco	Toxicity per kilo of animal	% Pyridine
Kentucky	5.33	0.48%
Egyptian	2.22	1.08%
Turkish	3.00	0.76%

(28) The result is thus that blond tobacco, not only produces more tar, but is also more toxic than black tobacco.

EXPERIMENTS WITH BLOND TOBACCO TAR

(29) The experiments were conducted on rabbits, by daily applications on the inner surface of the ear, in a limited area.

(30) The first manifestations in the tissue are observed, generally, between 5 and 6 months. (31) Hyperkeratous formations appear that are later transformed into keratous papillomas and even later, into an infiltrative carcinomas. (32) This evolution is reached within one year of treatment.

(33) There is in this process an evolution of lesions that a swelling of the skin begins, with a marked hyperplasia of the Malpighian body, which is already observed by the 2nd month. (34) This concerns a hyperplasia that thickens afterwards into an intense hard protrusion (hyperkeratosis), which posteriorly, forms a tree-like papillomatosis. (35) Microphotograph Nos. 1, 2 and 3.

(36) These are precancerous lesions. (37) If, during this period of the process, the tobaccular action is suppressed, the lesions will go into remission and can disappear. (38) If treatment is continued, definitive cancerization will set in, with infiltration and destruction of the organ.

(39) Two groups of rabbits were used for this experiment: one group treated with Egyptian tobacco tar and the other with Turkish tobacco tar.

(40) The results obtained are summarized below.

EXPERIMENT NO. 1

With Egyptian tobacco tar

(41) The experiment begins on March 15th, 1937 by applying tar in the right ear of 10 rabbits; 4 of these animals died two months later from the effects of intoxication, and they were replaced.

(42) Tumors have developed in 8 rabbits, or 80%.

(43) The initiation of this process has been variable; in No. 1 and No. 7 this has been precocious, since by the 49th and 56th days respectively the first papillomas had developed.

(44) In other animals, this period has been longer, from 100 to 280 days.

The results of this experiment are summarized below:

Rabbit No.	Time Elapsed Before the appearance of the the initial lesion	Tumors Developed in the ear
1	49 days	1
2	282 "	3
3	42 "	1
4	282 "	1
5	103 "	2
6	55 "	2
7	46 "	3
8	89 "	2
9	--	--
10	--	--

EXPERIMENT NO. 2

With Turkish Tobacco

Group of 10 rabbits.

(45) In this group, tumors developed in 9 animals, or 90%.

(46) The first lesions appeared in some animals between 60 and 90 days; in others these were produced later, 200 days before the first papillomas were noted.

(47) One of these rabbits, no. 2, photograph no. 1, which is the one whose lesions appeared with the most precocity (at 30 days), is also the one which developed the most tumors, reaching at 14 months a development of 9 tumors, 2 of which were very voluminous.

(48) The results are summarized in the following chart:

Rabbit No.	Time elapsed before the appearance of the initial lesion	Tumors Developed in the ear
1	97 days	2
2	218 "	1
3	141 "	2
4	141 "	2
5	270 "	2
6	108 "	3
7	129 "	2
8	63 "	9
9	74 "	3
10	--	--

(49) In the histology of the developed tumors, distinct evolutionary stages are observed. (50) Thus in the first two or three months one sees a more or less uniform epithelial hyperplasia on the skin of the treated ear, while the ear on the other side keeps its normal characteristics (microphotograph No. 1). (51) From 5 to 6 months, one observes the pronounced keratous formations of papillomas (microphotograph No. 2), and finally, cancerization sets in which is characterized by the growth of infiltration and in profundity of the epithelia, which acquires markedly anaplasial characteristics (microphotographs Nos. 3, 4, 5 and 6).

(52) It is possible to observe these distinct states of the process in the same ear, in such a manner that, near an area of hyperkeratosis, one sees some papillomas and a carcinoma.

The experiment previously described indicates:

(53) 1. that the blond tobacco studied not only produced a greater quantity of tar than the black tobacco, but also that this tar is more toxic. (54) It is these two findings that make blond tobacco a more dangerous product than black tobacco.

(55) 2. that the tar in blond tobacco produces a carcinogenic action similar to that of black tobacco.

(56) If one takes into account the number of tumors produced in the treated animals, one observes that the percentage of cancerous animals is high, from 80 to 90%.

(57) I relate the carcinogenic action of the tar in these tobaccos, as I have already indicated for black tobacco, to the presence of bodies of condensed benzene nuclei, of hydrocarbons of the aromatic group.

(58) This is a question of much interest that we have studied spectrographically for its absorption of ultraviolet rays, causing, even in very diluted solutions, 3.870 angstrom units which coincides with the absorption range of the mentioned hydrocarbons, which I have studied in detail in an earlier work (2).

(2) ROFFO, A.E. (Jr.), Spectrography of the derivatives obtained by the direct distillation of tobaccos and their relation to carcinogenic agents. In *Dol. del Inst. de Med. Exp.*, No. 45, pg. 297.

(59) Furthermore, we are dealing with a substance that is characterized by a fluorescence of a navy blue, almost violet color, which is also a characteristic of the fluorescence of 1-2 benzopyrene, 1-2 benzoanthracene and 1-2-5-6- debenzoanthracene (see Boletín del Inst. de Med. Exp., no. 42, pg. 307).

(60) In conclusion, we must add that these experimental results, which attribute a strong carcinogenic power to blond tobaccos, indicate as a consequence that the anticancerous prophylaxis must be intensified, extenuating the habit of smoking, especially in women, who have come to smoke these tobaccos excessively.

(61) If one takes into account that one kilo of these tobaccos produces 70 grams of tar, it is easy to imagine the consequences that this resinous complex has produced in the respiratory tracts, especially if one considers that a moderate smoker, from 2 to 3 packs a day, ends up smoking a kilo of tobacco per month, that is to say, deposits 70 grams of tar a month, and 840 grams a year on his mucous membranes.

(62) It is alarming to think that if a daily application on the epithelia of a rabbit's ear, which is much more resistant due to its keratous mantle than the mucous membrane of the mouth, larynx and bronchial tracts, produces a carcinoma in 9 months, with a total of 10 grams of tar, a smoker has many possibilities of cancerizing his mucous membranes, when in the same period of time he absorbs a quantity 80 times greater.

(Photographs)

1. Spectrogram in the ultraviolet range, of Egyptian tobacco tar with absorption bands.
2. Spectrogram in the ultraviolet range, of Turkish tobacco tar.
3. Spectrogram in the ultraviolet range, of Kentucky tobacco tar.
4. Graph of the ultraviolet absorption of Kentucky, Turkish and Egyptian tobacco tars.

Kentucky tobacco
Egyptian tobacco
Turkish tobacco

Experiment No. 1

Rabbit No. 1 - Carcinoma produced on the inner surface of the ear by Egyptian tobacco tar. T, voluminous tumor.

Rabbit No. 7 - Carcinoma produced on the inner surface of the ear by Egyptian tobacco tar. B., vegetative tumors.

Experiment No. 2

Rabbit No. 8 - Carcinoma produced on the inner surface of the rabbit's ear by Turkish tobacco tax. A. infiltrative carcinoma; B. 7 new papillomas; T. voluminous, vegetative, carcinogenic tumor.

Microphotograph No. 1 - Rabbit's ear treated with Egyptian tobacco tar. Epithelial hyperplasia at 2 months.

Microphotograph No. 2 - The previous rabbit at 4 months.

Intense hyperkeratosis and papillomatosis.

Microphotograph No. 3 - Rabbit's ear treated with Turkish tobacco tar; at 7 months. Papilloma with intense keratous protrusions.

Microphotograph No. 4 - Surface carcinoma developed in the ear with Egyptian tobacco tar. In (a), growth in profundity with marked anaplasia.

Microphotograph No. 5 - The previously prepared zone at greater magnification. ;

Microphotograph No. 6 - Carcinoma developed in the ear with Turkish tobacco tar.

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