

COMPARATIVE CHEMICAL ANALYSIS OF DIFFERENT LOTS OF ARIVA™

A. Appearance and Taste

To undertake a comparative chemical analysis of different lots of Ariva™, two different lots were purchased at a mini-mart store in the state of Virginia. Lot # 000102 (“#102”) was purchased in November 2001, while lot # 000110 (“#110”) was purchased in April 2002. The tobacco used in this analysis was obtained from a pack of Marlboro® cigarettes purchased in New Jersey in February 2002. Prior to conducting an analysis of the chemical and physical properties of these two lots of Ariva, the products’ physical appearance and taste were evaluated. As can be seen from Table 1, the principal conclusions from this evaluation are that the more recent formulation of Ariva consists of slightly smaller cigaletts™ that have a stronger mint/spearmint flavor.

Table 1. Appearance, Taste and Packaging

	Ariva (#102)	Ariva (#110)
Color	Dark Yellow to Brown	Dark Yellow to Brown
Weight	280 mg	250 mg
Flavor	Mint	Mint/Spearmint (intense)
Sweetener	Present	Present
Shape	Oval/debossed	Oval/debossed
Packaging	See through blister with Child Resistance Protection	See through blister with Child Resistance Protection
Dose	No dosage information	No dosage information

B. Disintegration and Hardness

The disintegration time and hardness of each lot of Ariva was also measured. Disintegration time is the time required for a cigalett to break down into smaller particles that are required for absorption into the human body. Prolonging the disintegration/dissolution time is an important factor for compounds such as nicotine since longer disintegration rates tend to yield greater absorption of the product. As shown in Table 2, this analysis found that the more recent lot of Ariva was harder and took substantially more time (i.e., almost 50% more time) to disintegrate.

Table 2. Disintegration and Hardness Properties

	Ariva (#102)	Ariva (#110)
Disintegration Time	18 minutes	26 minutes
Hardness (Strong-Cobb Hardness Units)	11 SC	13 SC

C. pH and Buffering Capacity

Inasmuch as the pH and buffering capacity of a product are also key factors in its absorption, the different lots of Ariva were also evaluated for these characteristics. Any pH above the pKa of a basic compound is required for faster absorption in the body. Nicotine has a pKa of 8.2, while lots 102 and 110 of Ariva have pKas of 8.4 and 8.6, respectively. In contrast, the tobacco used in this analysis has a pH of 5.6. Hence, as can be seen from the data in Table 3, it appears that Ariva has been specifically designed to maintain a high pH allowing for maximum nicotine absorption, and this is especially true of the more recent lot of Ariva.

This conclusion is bolstered by an analysis of the buffering capacity of the two lots of the product. The magnitude of the resistance of a buffer to pH changes is referred to as buffering capacity. Experiments utilizing human saliva were carried out with Ariva to estimate the buffering capacity of each lot. One ground cigarette from each lot was added to 10 ml of human saliva, and pH was recorded. As can also be seen from Table 3, the buffering capacity of Ariva is very high, especially for the more recent lot of the product. Thus, it appears that the product has been formulated, and reformulated, to create and maintain a pH and buffering capacity allowing for optimal absorption of nicotine.

Table 3. pH and Buffering Capacity (“BC”)

	Ariva (#102)	Ariva (#110)	Tobacco
pH	8.4	8.6	5.6
BC/cigarette	0.9 mmoles/L	1.3 mmoles/L	-
BC /gm of product	3.2 mmoles/L	5.0 mmoles/ L	4.1 mmoles/L

An analysis of certain inorganic compounds in Ariva further confirms that the product has been designed to facilitate maximum nicotine absorption. The two lots of Ariva were evaluated with Inductively Coupled Plasma detection. For further identification of calcium carbonate, infrared and Laser Raman spectroscopy techniques were also used. These analyses, as shown in Table 4, indicate that both lots of Ariva contain a similar percent of calcium carbonate, in spite of having different weights. This analysis also demonstrates that calcium carbonate is not a natural constituent of tobacco. Calcium carbonate is a part of a buffer system which would keep the pH high to enhance nicotine absorption. This analysis also found that the concentration of sodium in the more recent lot of Ariva has been reduced substantially and is only about a third of the concentration of sodium in the previous lot.

Table 4. Inorganic Compounds

	Ariva (#00102)	Ariva (#00110)	Tobacco
Calcium carbonate	18 %	18 %	0 %
Sodium (total)	2000 ppm	720 ppm	-

D. High Molecular Weight Ingredients

In addition to an evaluation of these physical properties, the two different lots of Ariva were chemically analyzed and compared. Samples of cigarettes from each lot of Ariva were analyzed using Size Exclusion Chromatography to determine the molecular weight of the ingredients present in the product. Although this technique is not capable of elucidating the molecular structure of a particular compound, it can provide an accurate estimate of the molecular weights of ingredients in the product. The results from this analysis, as illustrated in Table 5, indicate that both lots of Ariva have ingredients in the low molecular weight range similar to those in the reference tobacco product. Each lot of Ariva does contain, however, at least two additional ingredients, both with higher molecular weights, that are not found in the same concentrations as the reference tobacco product. One of these ingredients occurs in only relatively small quantities in the reference tobacco product, while the other was not detected at all.

The results from this analysis are consistent with GSK's earlier evaluation of Ariva, in which similar compounds were detected using the same analytical technique. Despite that earlier finding, however, Star has not (at least publicly) identified these compounds. Based on a review of the literature, the ingredient with a molecular weight of approximately 20,000 Daltons could be a pectin, which has previously been detected in tobacco. The other unknown ingredient with a molecular weight of 40,000+ Daltons could be a water-soluble polymer of natural or synthetic origin used during processing and manufacture of a cigarette. This conclusion would be consistent with the results obtained during the disintegration test that a significant polymer could be present in the formulation of Ariva.

Table 5. Molecular Weight Ingredients

Molecular Weight	Ariva (#102)	Ariva (#110)	Tobacco
1000 Daltons	Y	Y	Y
3500 Daltons	Y	Y	Y
4000 Daltons	Y	Y	Y
20,000 Daltons	Y (major)	Y (major)	Y (minor)
40,000+ Daltons	Y	Y	N

E. Nicotine Content

The average nicotine content in cigarettes from each lot of Ariva was also calculated through the use of gas chromatography. Both lots of Ariva were found to contain the same amount of nicotine per cigarette. However, because cigarettes in the more recent lot of Ariva (#110) have a lower average weight than those in the earlier Ariva lot (#102), they contain a greater concentration of nicotine. These results are depicted in Table 6.

Table 6. Nicotine Content

Amount Per Cigalett	Ariva (#102)	Ariva (#110)
	1.5 mg/cigalett	1.6 mg/cigalett
Amount Per Gram	(5.3 mg/g)	(6.4 mg/g)

F. Sugar Content

An analysis of the sugar content of the two different lots Ariva was also conducted. Size exclusion chromatography was used to separate and identify the sugars present in the different lots of Ariva. The results of this study are shown below in Table 7. The total amount of sugar in the more recent lot of Ariva is smaller than in the previous lot.

Table 7. Sugars

Sugar (mg/gram)	Ariva (#00102)	Ariva (#00110)
Fructose	27	20
Glucose	29	-
Sucrose	13	9

G. Principal Conclusions

In sum, the following conclusions have been drawn from the analysis described above. Ariva appears to have been reformulated so that cigaletts in more recent lots of the product: (a) are smaller and harder; (b) contain a more intense mint flavor; (c) do not disintegrate nearly as quickly as cigaletts from earlier lots; (d) maintain a higher pH and buffering capacity to allow for maximum absorption of nicotine; (e) provide a higher per unit dose of nicotine; (f) consist of slightly reduced levels of fructose and sucrose, and do not contain glucose; and (g) do not contain as much sodium as earlier lots of the product.