INTRODUCTION

As is well known nowadays, chlorogenic acids (CGAs) are naturally occurring compounds found in all higher plants. It is a family of esters formed between quinic and certain cinnamic acids. However, in spite of the “chloro” in the name, chlorogenic acids do not contain chlorine. This name comes from the Greek, which means light green. This is most likely because of the green color produced when the compounds are oxidized. CGAs are widely recognized to have many beneficial properties such as antioxidant activity, anticarcinogenic potential and may also slow the release of glucose into the bloodstream after a meal. Also, they have strong anti-inflammatory, anti-bacterial and anti-obesity properties. Because of these many positive influences on human body, since the middle of the 19th century, when the first references about CGAs appeared, there have been a high amount of articles dealing with extraction and detection techniques of CGAs or studying their influence on human health. CGAs have been observed and isolated in many plant materials such as coffee, apple, tomato, papaya, sweet potato, prune, pear, cabbage, yacon, burdock, cherry, apricot, orange, etc. Coffee beans are undoubtedly the most common observed matrix because coffee is the main source of CGAs. In the final coffee beverage, content of CGAs is supposed to be responsible for cup quality. In potatoes, for instance, the compounds are considered to cause undesirable “after-cooking blackening or darkening”; in other words, they seem to be responsible for bluish-grey discoloration of potatoes exposed to air after boiling or steaming.

The main purpose of this work is not to bring up some other new extraction or detection possibilities for obtaining CGAs from plant materials neither to reveal some new observed properties of these compounds. It is to point out the considerable differences in articles dealing with the chlorogenic acid esters. During last decade, there have been a high number of articles dealing with the family. Unfortunately, researchers who want to get knowledge about this topic may be strongly confused after reading a few articles. Due to gradual discoveries and isolations of the individual isomers from plenty of matrices and because of the changing system of terminology after these discoveries, discrepancies among articles are common. The cause of this confusion is that the main compound of the family, 5-caffeoylquinic acid (also well-known as chlorogenic acid), was truly called as 3-caffeoylquinic acid before 1976, when new rules for nomenclature were published. Many researchers and also chemicals suppliers, however, keep using the “pre-IUPAC” nomenclature and wrongly call 3-caffeoylquinic acid as chlorogenic acid, the main substituent of the family. Despite there have been some works struggling with this issue, the problem is still appearing. Therefore, the present work was written.

**Keywords:** chlorogenic acid; neochlorogenic acid; nomenclature; coffee.
described and isolated from Elberta and Halford peaches as a crystalline material by Corse in 1953. In 1955, Uritani and Miyano succeeded with the isolation of pseudochlorogenic acid (1-CQA) from sweet potatoes infected with black rot. The last possible mono isomer got the name cryptochlorogenic acid (4-CQA) and it was explored and isolated in 1964 by Waiss. These two acids are very easy to distinguish due to the fact their OH groups are placed directly across from the carbon carrying the COOH group or exactly at the carbon carrying the COOH group, respectively.

Also, in 1950, Barnes et al. described a compound with a trivial name: isochlorogenic acid. This compound was isolated from coffee beans and it was reported to have similar properties as CQA. The authors determined this compound as a position isomer of chlorogenic acid, which is based on the same molecular weight, ultimate composition, hydrolysis compound or similar UV and IR spectra. Unlike CQA, isochlorogenic acid does not form a complex analogous to the crystalline potassium chlorogenate. Nowadays, the term isochlorogenic acid is used for polyphenolic compounds which are composed of quinic acid and two caffeic acids (di-CQA).

**NOMENCLATURE**

**Problems with the numbering**

As said in the Introduction, the main goal of this article is to point out the big problems and common disagreements in the nomenclature of chlorogenic acids isomers. At the very beginning, it has to be announced that the name chlorogenic acid should not be used only for one compound but it should describe one or more family of esters that form between certain cis- or trans-cinnamic acids, mostly caffeic, ferulic or p-coumaric (see figure 1), and quinic acid. For instance, CGAs composition of coffee, one of the most popular beverages in the world, is complex with at least 5 major groups of compounds present. Those are caffeoylquinic acids (CQA), dicaffeoylquinic acids (diCQA), feruloylquinic acids (FQA), p-coumaroylquinic acids (CoQA) and caffeoylferuloylquinic acids (CFQA). In Table 1 and Figure 2 are shown the most common studied types of CGAs composition with correct abbreviations.

The biggest discrepancies are with the designation of two compounds belonging among the caffeoylquinic acids, the 5-CQA and 3-caffeoylquinic acid (3-CQA), which are often commuted. If trivial names are used, it is usual to call them chlorogenic acid and neochlorogenic acid, respectively. Those are optical isomers that are very difficult to distinguish if researchers are not well-acknowledged with their nomenclature (see below). Figure 3 clearly shows if a spatial structure for illustration of chlorogenic acid is not used, there is no possibility of recognizing the two above mentioned enantiomers between each other. Furthermore, some authors use such figures in their articles, which can be seen, for instance, in the works of Mills et al. or De Maria et al. This problem is also common in a plenty of research and web pages. However, according to International Union of Pure and Applied Chemistry (IUPAC) numbering system published in 1976, there are strict rules, which makes easier to differentiate these two enantiomers.

**Figure 2.** 2-D structure of a compound which could be named 3-CQA or 5-CQA

**Quinic acid according to IUPAC**

As was mentioned, CGAs are composed by various types of trans-cinnamic acids always bound to quinic acid. It has to be stated the latter one could be incorrectly considered as a saccharide. However, it is a type of cyclitol which are generally not regarded to be a carbohydrate. Because of that, the nomenclature for cyclitols deals with another rules described in the IUPAC system recommendation. Therefore, the numbering system of CGAs is related to the numbering of cyclitols that was suggested by Maquenne in 1900. He proposed a fractional notation, where numerals in the numerator denote hydroxyl or other group (with exception of hydrogen) above the plane of the ring and numerals in the dominator denote hydroxyl

Table 1. Various types of substitution of quinic acid with caffeic, ferulic or p-coumaric acid

| Compound abbreviation | Identity of R3 | Identity of R4 | Identity of R5 |
|-----------------------|----------------|----------------|----------------|
| 3-CQA                 | caffeic acid   | hydrogen       | hydrogen       |
| 4-CQA                 | hydrogen       | caffeic acid   | hydrogen       |
| 5-CQA                 | hydrogen       | hydrogen       | caffeic acid   |
| 3-FQA                 | ferulic acid   | hydrogen       | hydrogen       |
| 4-FQA                 | hydrogen       | ferulic acid   | hydrogen       |
| 5-FQA                 | hydrogen       | hydrogen       | ferulic acid   |
| 3-p-CoCQA             | p-coumaric acid| hydrogen       | hydrogen       |
| 4-p-CoCQA             | hydrogen       | p-coumaric acid| hydrogen       |
| 5-p-CoCQA             | hydrogen       | hydrogen       | p-coumaric acid|
| 3,4-diCQA             | caffeic acid   | caffeic acid   | hydrogen       |
| 3,5-diCQA             | caffeic acid   | hydrogen       | caffeic acid   |
| 4,5-diCQA             | hydrogen       | caffeic acid   | caffeic acid   |
| 3,4-CFQA              | ferulic acid   | ferulic acid   | hydrogen       |
| 3,5-CFQA              | ferulic acid   | hydrogen       | ferulic acid   |
| 4,5-CFQA              | hydrogen       | caffeic acid   | ferulic acid   |
| 3,4-CFQA              | ferulic acid   | caffeic acid   | hydrogen       |
| 3,5-CFQA              | ferulic acid   | hydrogen       | ferulic acid   |
| 4,5-CFQA              | hydrogen       | caffeic acid   | ferulic acid   |

**Figure 3.** 2-D structure of a compound which could be named 3-CQA or 5-CQA

**Figure 1.** Structural formulas of quinic acid (a) and three most common trans-cinnamic acids of CGAs family: caffeic acid (b), ferulic acid (c) and p-coumaric acid (d)
or other group (with exception of hydrogen) below the plan of the ring. However, Maquenne did not specify the exact way of allocation of the numerals to the specific positions. Afterwards, Posternak developed another system of numbering which was very popular to use until the above-mentioned year 1976, when the IUPAC system for nomenclature of cyclitols was published. Lower in that paper is exactly described how the quinic acid ring should be numbered.33

In the literature, there can be found names like D-quinic or L-quinic acid. As is well known, these symbols label whether the configuration at the reference carbon in the Fischer projection is the same (or the opposite) as that one in the D-(+)-glyceraldehyde.43,44 However, this is an old labeling which occurs mostly with names of natural compounds (or substrutents made from natural compounds). Nowadays, enantiomers are distinguished as R- and S- isomers. This system is sometimes called the CIP (as the abbreviation of three authors - Cahn, Ingold, Prelog - who suggested this system) or the R-S system. Also, it is possible to meet names like (-)-Quinic acid or (+)-Quinic acid. Those symbols introduce only information about rotation of plane of polarized light.

According to papers, however, it is (-)-quinic acid or D-(+)-quinic acid, which results in different types of CGAs by its conjugation with one or more of the above-named trans-cinnamic acids.45-47 In the IUPAC system, D-(+)-quinic acid is defined as 1L1(OH)3,4/5-tetrahydroxycyclohexanecarboxylic acid. Regarding the R-S system, the name of this acid is (1S,3R,4S,5R)-1,3,4,5-tetrahydroxyclohexanecarboxylic acid.

As was already written, the biggest problems are with the commutation of 5-CQA and 3-CQA. Nowadays, both of these compounds are available in a pure crystal form purchasable from commercial suppliers. Unfortunately, majority of the suppliers keep the pre-IUPAC nomenclature and sell chlorogenic acid as 3-caffeoylquinic acid. This is probably because of the fact that in 1976, when IUPAC numbering system for cyclitols was published, the name for chlorogenic acid was really 3-caffeoylquinic acid and pure form of neochlorogenic acid was not yet purchasable.

The evidence of unremitting wrong nomenclature can be found in recent studies.48-52 Besides, in a work of Moeenfard et al.,51 the problems with nomenclature are rightly mentioned and pointed out, although these same authors also used the wrong one. Furthermore, in the discussion they wondered about their results, dealing with CGAs contained in coffee brews, and compared them to the results published in other papers. Some of them are in agreement with Moeenfard’s results and some are not. The work in compliance was published by Gloess et al.,52 but they also used the wrong nomenclature. Both of these authors mentioned 3-CQA as chlorogenic acid. Therefore, according to them, 3-CQA was the most abundant compound. On the other hand, in the other compared work of Fujioka,53 the main compound observed was 5-CQA. Fujioka, however, did not use trivial names. From the mentioned is obvious that authors compared different compounds – chlorogenic and neochlorogenic acid.

According to the current rules, however, the structure of chlorogenic acid for the reason of this term should definitely be 5-CQA. Hence it is clear that 3-CQA is an abbreviation for neochlorogenic acid. These results have to be considered by researchers if CGAs are targets of the research.

CONCLUSION

This short review has been written due to an obvious and unremitting wrong nomenclature occurring in chlorogenic acid family. These discrepancies are caused by the fact that 5-caffeoylquinic acid (5-CQA) was firstly discovered and subsequently isolated already in the middle of 19th century. However, from that time up to 1976, when IUPAC published the exact rules and definitions describing a new system of nomenclature, the right name for the current 5-CQA was actually 3-caffeoylquinic acid. In spite of that fact, researchers and also chemicals suppliers have been still using this pre-IUPAC nomenclature. Therefore, the authors of the present article expect that this work will help further researchers to avoid any mistakes and disagreements, so it could be much easier to correctly compare different studies dealing with the chlorogenic acid family.

REFERENCES

1. Clifford, M. N.; J. Sci. Food. Agr. 1999, 79, 362.
2. Clifford, M. N.; Wu, W. G.; Kuhnert, N.; Food Chem. 2006, 95, 574.
3. Hahgi, G.; Hatami, A.; Arshi, R.; Food Chem. 2011, 124, 1029.
4. Bakuradze, T.; Boehm, N.; Janzowskii, C.; Lang, R.; Hofmann, T.; Stockis, J. P.; Albert, F. W.; Steibitiz, H.; Bytof, G.; Lantzi, I.; Baum, M.; Eisenbrand, G.; Mol. Nutr. Food Res. 2011, 55, 793.
5. Tunncliffe, J. M.; Eller, L. K.; Reimer, R. A.; Hittel, D. S.; Shearer, J.; Appl. Physiol. Nutr. Metab. 2011, 36, 650.
6. Chagas-Paula, D. A.; de Oliveira, R. B.; da Silva, V. C.; Gobbo-Neto, L.; Gasparoto, T. H.; Campanelli, A. P.; Faccioli, L. H.; Da Costa, F. B.; J. Ethnopharmacol. 2011, 136, 355.
7. Cho, A. S.; Jeon, S. M.; Kim, M. J.; Yeo, J.; Seo, K. I.; Choi, M. S.; Lee, M. K.; Food Chem. Toxicol. 2010, 48, 937.
8. Wang, G. F.; Shi, L. P.; Ren, Y. D.; Liu, Q. F.; Liu, H. F.; Zhang, R. J.; Li, Z.; Zhu, F. H.; He, P. L.; Tang, W.; Tao, P. Z.; Li, Z.; Zhao, W. M.; Zuo, J. P.; Antiviral Res. 2009, 83, 186.
9. Ludwig, L. A.; Mena, P.; Calani, L.; Ciú, C.; Del Rio, D.; Lean, M. E. J.; Cribzer, A.; Food Fuct. 2014, 5, 1718.
10. Liandmanskas, M.; Viskelis, P.; Kviklys, D.; Raudonis, R.; Janulis, V.; Int. J. Food Prod. 2015, 18, 945.
11. Siriamornpun, S.; Rasteejo, W.; Kaewsejwan, N.; Meeso, N.; Rsc. Adv. 2015, 5, 18579.
12. Sasaki, K.; Oki, T.; Kobayashi, T.; Kai, Y.; Okuno, S.; Biosci., Biotechnol., Biochem. 2014, 78, 2073.
13. Jabeen, Q.; Aslam, N.; J. Med. Plants Res. 2011, 5, 1508.
14. Lee, S. W.; Lee, Y. G.; Cho, J. Y.; Kim, Y. C.; Lee, S. H.; Kim, W. S.; Moon, J. H.; J. Korean Soc Appl. Biol. Chem. 2015, 58, 335.
15. Fernandez-Leon, A. M.; Lozano, M.; Gonzalez, D.; Ayuso, M. C.; Fernandez-Leon, M. F.; Czech. J. Food Sci. 2014, 32, 549.
16. Oliveira, R. B.; Chagas-Paula, D. A.; Secatto, A.; Gasparoto, T. H.; Facioli, L. H.; Campanelli, A. P.; Da Costa, F. B.; Rev. Bras. Farmacogn. 2013, 23, 497.
17. Tang, Y. X.; Lou, Z. X.; Yang, L.; Wang, H. X.; Eur. Food Res. Technol. 2015, 240, 1203.
18. Xiao, Z. B.; Fang, L. L.; Niu, Y. W.; Yu, H. Y.; Food Chem. 2015, 186, 69.
19. Kan, T.; Gundogdu, M.; Ercisli, S.; Muradoglu, F.; Celik, F.; Gecer, M. K.; Kodad, O.; Zia-Ul-Haq, M.; Biol. Res. 2014, 47.
20. Agcam, E.; Akyildiz, A.; Evrendilek, G. A.; K.; Kodad, O.; Zia-Ul-Haq, M.; Biol. Res. 2014, 47.
21. Agcam, E.; Akyildiz, A.; Evrendilek, G. A.; Food Chem. 2014, 143, 354.
22. Bassoli, B. K.; Cassolla, P.; Borba-Murad, G. R.; Constantine, J.; Salgueiro-Pagadigorría, C. L.; Bazotte, R. B.; de Souza, H. M.; Cell. Biochem. Fuct. 2015, 33, 183.
23. Farah, A.; Monteiro, M. C.; Calado, V.; Franca, A. S.; Trugo, L. C.; Food Chem. 2006, 98, 373.
24. Hao, D.; Friedman, M.; J. Agric. Food Chem. 1992, 40, 2152.
25. Swain, T., Economic importance of flavonoid compounds: foodstuffs. 1962, Pergamon Press, Oxford.
26. Robiquet; Ann. Pharm. 1837, 3, 93.
27. Payen, A.; Compte-Rendus de l’Académie des Sciences (Paris) 1846, 22, 724.
28. Hardy, F.; Warneford, F. H. S.; Ind. Eng. Chem. 1925, 17, 48.
29. Hulme, A. C.; Biochem. J. 1953, 53, 337.
29. Moores, R. G.; McDermott, D. L.; Wood, T. R.; *Anal. Chem.* 1948, 20, 620.
30. Charaux, C.; *J. Pharm. Chim.* 1910, 102, 292.
31. Thomas, A. W.; *J. Ind. Eng. Chem.-U.S.* 1922, 14, 829.
32. Feldman, J. R.; Ryder, W. S.; Kung, J. T.; *J. Agric. Food Chem.* 1969, 17, 733.
33. Corse, J.; *Nature* 1953, 172, 771.
34. Uritani, I.; Miyano, M.; *Nature* 1955, 175, 812.
35. Waiss, A. C.; Lundin, R. E.; Corse, J.; *Chem. Ind.* 1964, 1984.
36. Barnes, H. M.; Feldman, J. R.; White, W. V.; *J. Am. Chem. Soc.* 1950, 72, 4178.
37. Guo, W.; Wang, L.; Gao, Y.; Zhao, B.; Wang, D.; Duan, W.; Yu, Z.; *J. Chromatogr. B* 2015, 981–982, 27.
38. Clifford, M. N.; Wight, J.; *J. Sci. Food Agric.* 1976, 27, 73.
39. Clifford, M. N.; Johnston, K. L.; Knight, S.; Kuhnert, N.; *J. Agric. Food Chem.* 2003, 51, 2900.
40. Mills, C. E.; Oruna-Concha, M. J.; Mottram, D. S.; Gibson, G. R.; Spencer, J. P. E.; *Food Chem.* 2013, 141, 3335.
41. De Maria, C. A. B.; Moreira, R. F. A.; *Quim. Nova* 2004, 27, 586.
42. IUPAC Commission on the Nomenclature of Organic Chemistry (CNOC); IUPAC-IUB Commission on Biochemical Nomenclature (CBN); *Biochem. J.* 1976, 153, 23.
43. De Azevedo, W. F.; Lecerc; S.; Havlicek; L.; Strnad, M. H.; *Eur. J. Biochem.* 1997, 243, 518.
44. IUPAC Commission on the Nomenclature of Organic Chemistry (CON); IUPAC-IUB Commission on Biochemical Nomenclature (CBN); *Arch. Biochem. Biophys.* 1968, 128, 269.
45. Kovacs, L.; *Magy. Kem. Foly.* 1997, 103, 178.
46. Cahn, R. S.; Ingold, C.; Prelog, V.; *Angew. Chem. Int. Edit.* 1966, 5, 385.
47. Hemmerle, H.; Burger, H.-J.; Below, P.; Schubert, G.; Rippel, R.; Schindler, P. W.; Paulus, E.; Herling, A. W.; *J. Med. Chem.* 1997, 40, 137.
48. Farah, A.; De Paulis, T.; Trugo, L. C.; Martin, P. R.; *J. Agric. Food Chem.* 2005, 53, 1505.
49. Fu, X.; Yin, Z. P.; Chen, J. G.; Shangguan, X. C.; Wang, X. Q.; Zhang, Q. F.; Peng, D. Y.; *J. Agric. Food Chem.* 2015, 63, 262.
50. Sun, P. C.; Liu, Y.; Yi, Y. T.; Li, H. J.; Fan, P.; Xia, C. H.; *Food Chem.* 2015, 168, 55.
51. Moeenfard, M.; Rocha, L.; Alves, A.; *J. Anal. Methods Chem.* 2014, 2014, 965353.
52. Gloess, A. N.; Schonbachler, B.; Klopprogge, B.; D’Ambrosio, L.; Chatelain, K.; Borgartz, A.; Strittmatter, A.; Rast, M.; Yeretzian, C.; *Eur. Food Res. Technol.* 2013, 236, 607.
53. Fujioka, K.; Shibamoto, T.; *Food Chem.* 2008, 106, 217.