

REFERENCES

- [1] Pieters, L.; Vlietinck, A. J. Bioguided isolation of pharmacologically active plant components, still a valuable strategy for the finding of new lead compounds? *J Ethnopharmacol.* 100 (2005): 57-60.
- [2] Sporn, M. B.; Suh, N. Chemoprevention: An essential approach to controlling cancer. *Nat Rev Cancer.* 2 (2002): 537-43.
- [3] Rossa, S. A.; Ziskac, D. S.; Ke Zhaod & ElSohly, M. A. Variance of common flavonoids by brand of grapefruit juice. *Fitoterapia.* 71 (2000): 154–161.
- [4] Harborne, J. B.; Williams, C. A. Advances in flavonoid research since 1992. *Phytochemistry.* 55 (2000): 481–504.
- [5] Peterson, J.; Dwyer, J. Flavonoids: Dietary occurrence and biochemical activity. *Nutr. Res.* 18 (1998): 1995–2018.
- [6] Kurowska, E. M.; Borradaile, N. M.; Spence, J. D., & Carroll, K. K. Hypocholesterolemic effects of dietary citrus juices in rabbits. *Nutr. Res.* 20 (2000): 121–129.
- [7] Vinson, J. A.; Liang, X.; Proch, J.; Hontz, B. A.; Dancel, J.; Sandone, N. Polyphenol antioxidants in citrus juices: In vitro and in vivo studies relevant to heart disease. *Advances in Experimental Medicine and Biology.* 505 (2002): 113–122.
- [8] Benavente-Garcia, O.; Castillo, J.; Martin, F. R.; Ortuno, A.; Del Rio, J. A. Use and properties of *Citrus* flavonoids. *J. Agric. Food. Chem.* 27 (1997): 249-254.
- [9] Yu, J.; Wang, L.; Walzem, R. L.; Miller, E. G.; Pike, L. M.; Patil, B. S. Antioxidant activity of citrus limonoids, flavonoids, and coumarins. *J. Agric. Food. Chem.* 53 (2005): 2009–2014.
- [10] Deyhim, F.; Garcia, K.; Gonzalez, J.; Lopez, E.; Ino, S.; Garcia, M. et al. Citrus juice modulates bone strength in male senescent rat model of osteoporosis. *Nutrition.* 22 (2006): 559–563.

- [11] Deyhim, F.; Lopez, E.; Gonzalez, J.; Garcia, M.; Patil, B. S. Citrus juice modulates antioxidant enzymes and lipid profiles in orchidectomized rats. *J. Med. Chem.* 9 (2006): 422–426.
- [12] Rossa, S. A.; Ziskac, D. S.; Ke Zhaod & ElSohly, M. A. Variance of common flavonoids by brand of grapefruit juice. *Fitoterapia.* 71 (2000): 154–161.
- [13] Mouly, P. P.; Gaydou, E. M.; Faure, R.; Estienne, J. M. Blood orange juice authentication using cinnamic acid derivative. Variety differentiations associated with flavanone glycoside content. *J. Agric. Food. Chem.* 45 (1997): 373-377.
- [14] Rouseff, R. L. In Adulteration of fruit juice beverages. Differentiating citrus juices using flavanone glycoside concentration profiles. New York: Dekker, 1988.
- [15] Rouseff, R. L.; Martin, S. F.; Youtsey, C. O. Quantitative survey of narirutin, naringin, hesperidin and neohesperidin in citrus. *J. Agric. Food Chem.* 35 (1987): 1027-1030.
- [16] Kefford, J. F. In Advances in food research The chemical constituents of citrus fruits. Academic Press: New York, 1959, 286-354.
- [17] Jordan, P. S.; Weiler, E. W.; Mansell, R. L. Radioimmunoassay for naringin and related flavanone 7-neohesperidosides using a tritiated tracer. *J. Agri. Food. Chem.* 31 (1983): 1249-1255.
- [18] Joshipura, K. J.; Hu, F. B.; Manson, J. E.; Stampfer, M. J.; Rimm, E. B.; Speizer, F. E. et al. The effect of fruit and vegetable intake on risk for coronary heart disease. *Ann. Inter. Med.* 134 (2001): 1106–1114.
- [19] Swingle, W.T.; Reece, P.C. In The Citrus Industry. I Vol. The botany of *Citrus* and its wild relatives. University of California Press, 1967.

- [20] Swingle, W.T. In The Citrus Industry. I Vol. The botany of *Citrus* and its wild relatives of the orange subfamily. University of California Press: 1943, 129–474.
- [21] Izquierdo, L.; Sendra, J. M. In B., Encyclopedia of food science and nutrition. Citrus fruits composition and characterization. Oxford: Academic Press: 2003.
- [22] Cohn, R.; Cohn, A. L. Subproductos del procesado de las frutas. Spain: 1997, 288.
- [23] Caristi, C.; Bellocchio, E.; Panzera, V.; Toscano, G.; Vadala', R.; Leuzzi, U. Flavonoids detection by HPLC-DAD-MS-MS in lemon juice from Sicilian cultivars. J. Agric. Food Chem. 51 (2003): 3528-3534.
- [24] Manthey, J. A.; Grohmann, K. Phenol in citrus peel byproducts: concentrations of hydroxylcinnamates and polymethoxylated flavones in citrus peel molasses. J. Agric. Food. Chem., 49 (2001): 3268.
- [25] Sinclair, W. B. 1984. The Biochemistry and Physiology of the Lemon and Other Citrus Fruits. Division of Agriculture and Natural Resources, University of California: Oakland.
- [26] Horowitz, R. M. In The Orange. Its Biochemistry and Physiology, The citrus flavonoids. University of California, Division of Agricultural Science: Los Angeles, 1961, 334-372.
- [27] Bocco, A.; Cuvelier, M. E.; Richard, H.; Berset, C. Anti-oxidant activity and phenolic composition of citrus peel and seed extracts. J. Agric. Food. Chem. 46 (1998): 2123–2129.
- [28] Gorinstein, S.; Zachwieja, Z.; Katrich, E.; Pawelzik, E.; Haruenkit, R.; Trakhtenberg, S. et al. Comparison of the contents of the main antioxidant compounds and the antioxidant activity of white grapefruit and his new hybrid. LWT--Food Sci. Technol. 37 (2004): 337–343.
- [29] Laufenberg, G.; Kunz, K.; Nystroem, M. Transformation of vegetable waste into value added products: (A) the upgrading concept; (B) practical implementations. Bioresour. Technol. 87 (2003): 167–198.

- [30] Leuzzi, U.; Caristi, C.; Panzera, V.; Licandro, G. Flavonoids in pigmented orange juice and second-pressure extracts. *J. Agric. Food Chem.* 48 (2000): 5501-5506.
- [31] Manthey, J. A.; Grohmann, K. Concentration of hesperidin and other orange peel flavonoids in citrus processing byproducts. *J. Agric. Food Chem.* 44 (1996): 811-814.
- [32] El-Nawawi, S. A.; Heikal, Y. A. Production of a low ester pectin by deesterification of high ester citrus pectin. *Carbohydr. Polym.* 27 (1995): 191-195.
- [33] Graham, R. P.; Shepherd, A. D. Pectin production-pilot plant production of low-methoxyl pectin from citrus peel. *J. Agric. Food Chem.* 1, 16 (1953): 993-1001.
- [34] Kawaii, S.; Tomono, Y.; Katase, E.; Ogawa, K.; Yano, M. Quantitation of flavonoid constituents in citrus fruits. *J. Agric. Food. Chem.* 47 (1999): 3565-3571.
- [35] Horowitz, R. M. Biochemistry of phenolic compounds. Academic Press: New York, 1964, 545.
- [36] Burda, S.; Oleszek, W. Antioxidant and Antiradical Activities of Flavonoids. *J. Agric. Food. Chem.* 49 (2001): 2774-2779.
- [37] Aboobaker, V.S.; Balgi, A.D.; Bhattacharya, R.K. In vivo effect of dietary factors on the molecular action of aflatoxin B1: Role of non-nutrient phenolic compounds on the catalytic activity of liver fraction. *In Vivo*, 8 (1994); 1095-1098.
- [38] Kaul, T. N.; Middleton Jr. E.; Ogra, P.L. Antiviral effect of flavonoids on human viruses. *J. Med. Virol.* 15 (January 1985): 71-79.
- [39] Murray, G. I.; Burke, D. M. Immunohistochemistry of drug-metabolizing enzymes. *Biochem. Pharmacol.* 50 (1995): 895-903.

- [40] Spatzenegger, M.; Jaeger, W. Clinical importance of hepatic cytochrome P450 in drug metabolism. Drug Metab Rev. 27 (1995):397-417.
- [41] Meyer U. A. Overview of enzymes of drug metabolism. J Pharmacokinet Biopharm. 24 (1996): 449-59.
- [42] Wrighton, S. A.; VandenBranden, M.; Ring, B. J. The human drug metabolizing cytochromes P450. J. Pharmacokinet. Biopharm. 24 (1996): 461–473.
- [43] Gonzalez, F. J.; Gelboin, H. V. Role of human cytochromes P450 in the metabolic activation of chemical carcinogens and toxins. Drug Metab Rev. 26 (1994):165-183.
- [44] Kerremans, A. L. Cytochrome P450 isoenzymes--importance for the internist, Neth J Med. 48 (1996): 237-243.
- [45] Pirmohamed, M.; Kitteringtam, N. R.; Park, B. K. The role of active metabolites in drug toxicity. Drug Saf. 11 (1994):114-44.
- [46] Ueng, Y. F.; Chang, Y.L.; Oda, Y.; Park, S.S.; Liao, J.F.; Lin, M.F.; Chen, C.F. In vitro and in vivo effects of naringin on cytochrome P450-dependent monooxygenase in mouse liver. Life Sci. 65 (1999): 2591-2602.
- [47] Kumar, G.N.; Walle, U.K.; Walle, T. Cytochrome P450 3Amediated human liver microsomal taxol 6_-hydroxylation. J. Pharmacol. Exp. Ther. 268 (1994): 160–165.
- [48] Peter, H.; Pavel, T.; Marie, S. Flavonioids-potent and versatile biologically active compounds interacting with cytochrome P450. Chemico-biol. Interact. 139 (2002): 1–12.
- [49] Doostdar, H.; Burke, M.D.; Mayer, R.T. Bioflavonoids: selective substrates and inhibitors for cytochrome P450 (CYP1A and CYP1B1). Toxicology. 144 (2000): 31–38.
- [50] Hodek, P.; Trefil, P.; Stiborova, M. Flavonoids-potent and versatile biologically active compounds interacting with cytochrome P450. Chem. Biol. Interact. 139 (2002): 1–21.

- [51] Maridonneau-Parini I.; Braquet, P.; Garay, R. P. Heterogeneous effect of flavonoids on k+-loss and lipid peroxidation induced by oxygen free radicals in human red cells. Pharmacal. Res. Commun. 18 (1986): 61-72.
- [52] Borradaile, N. M.; Carroll, K. K.; Kurowska, E. M. Regulation of HepG2 cell apolipoprotein B metabolism by the citrus flavonones hesperitin and naringenin. Lipids. 34 (1999): 591-598.
- [53] Kanno, S.; Shoji, A.; Asou, K.; Ishikawa, M. Effects of naringin on hydrogen peroxide-induced cytotoxicity and apoptosis in p388 cells. J. Pharmacal. Sci. 92 (2003): 166-170.
- [54] Kanno, S.; Shouji, A.; Hirata, R.; Asou, K.; Ishikawa, M. Effects of naringin on cytosine arabinoside (Ara-C)-induced cytotoxicity and apoptosis in P388 cells. Life sci. 75 (2004): 353-365.
- [55] So, F.V.; Guthrie, N.; Chambers, A.F.; Moussa, M.; Carroll, K.K. Inhibition of human breast cancer cell proliferation and delay of mammary tumorigenesis by flavonoids and citrus juices. Nutr. Cancer. 26 (1996): 167–181.
- [56] Puri, M.; Marwaha, S. S.; Kothari, R. M.; Kennedy, J. F. Studies on the applicability of alginate-entrapped naringiase for the debittering of kinnow juice. Enzyme Microb. Technol. 18 (1996): 281.
- [57] Booth, A. N.; Jones, F. T.; DeEds, F. Metabolic and glucosuria studies on naringin and phloridzin. J. Biol. Chem. 233 (1958): 280-282.
- [58] Ameer, B.; Weintraub, R. A.; Johnson, J. V.; Yost, R. A.; Rouseff, R. L. Flavanone absorption after naringin, hesperidin, and citrus administration. Clin. Pharmacol. Ther. 60 (1996): 34-40.
- [59] Braverman: J. B. S.? Citrus Products. Interscience, New York: 1949, 98.
- [60] Kesterson, J. W., Hendrickson, R., Florida Agr. Expt. Sta., Tech. Bull. 511, 1953.
- [61] Hodgson, R. W. In The Citrus Industry. Horticultural varieties of *Citrus*. University of California Press: Berkeley, 1967, 431-531.

- [62] Available from: <http://th.wikipedia.org>
- [63] Available from: <http://images.google.co.th>
- [64] Available from: <http://www.doa.go.th>
- [65] Ortúñ, A.; García-Puig, D.; Fuster, M. D.; Pérez, M. L.; Sabater, F.; Porras, I.; García-Lindón, A.; Del Río, J. A. Flavanone and nootkatone level in different varieties of grapefruit and pummelo. *J. Agri. Food Chem.* 43 (1995): 1-5.
- [66] Gorinstein, S.; Martín-Belloso, O.; Park, Y. S.; Haruenkit, R.; Lojek, A.; Čiž, M.; caspi, A.; Libman, I.; Trakhtenberg, S. Comparison of some biochemical characteristics of different citrus fruits. *Food Chemistry.* 74 (2001): 309-315.
- [67] Li, B.B.; Smith, B.; Hossain, Md. M. Extraction of phenolics from citrus peels I. Solvent extraction method. *Sep. Purif. Technol.* 48 (2006): 182–188.
- [68] Anagnostopoulou, M. A.; Kefalas, P.; Papageorgiou, V. P.; Assimopoulou, A. N.; Boskou, D. Radical scavenging activity of various extracts and fractions of sweet orange peel (*Citrus sinensis*). *Food chemistry.* 94 (2006): 19-25.
- [69] Peterson, J. J.; Dwyer, J. T.; Beecher, G. R.; Bhagwat, S. A.; Gebhardt, S. E.; Haytowitz, D. B.; Holden, J. M. Flavanones in oranges, tangerines (mandarins), tangors, and tangels: a compilation and review of the data from the analytical literature. *Food composition and analysis.* 19 (2006): 66-73.
- [70] Rehman, Z. Citrus peel extract – A natural source of antioxidant. *Food chemistry.* 99 (2006): 450-454.
- [71] Wu, T.; Guan, T.; Ye, J. Determination of flavonoids and ascorbic acid in grapefruit peel and juice by capillary electrophoresis with electrochemical detection. *Food chemistry.* 100 (2007): 1573–1579.
- [72] Abeysinghe, D. C.; Li, X.; Sun, C.; Zhang, W.; Zhou, C.; Chen, K. Bioactive compounds and antioxidant capacities in different edible tissues of citrus fruit of four species. *Food Chemistry.* 104 (2007): 1338-1344.

- [73] Jayaprakasha, G. K.; Girennavar, B.; Patil, B.S. Antioxidant capacity of pummelo and navel oranges: Extraction efficiency of solvents in sequence. LWT--Food Sci. Technol. 41 (2008): 376-384.
- [74] Marín, F. R.; Soler-Rivas, C; Benavente-García, O.; Castillo, J.; Pérez-Alvarez, J. A. By-products from different citrus processes as a source of customized functional fibres. Food Chemistry. 100 (2007): 736-741.
- [75] Kanaz, F. I.; Gabrieli, C.; Kokkalou, E.; Georgarakis, M.; Niopas, I. Simultaneous reversed-phase high-performance liquid chromatographic method for the determination of diosmin, naringin and hesperidin in different citrus fruit juices and pharmaceutical formulations. J. Pharmacal. Biomed. Anal. 33 (2003): 243-249.
- [76] Singleton, V. L.; Rossi, J. A. Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. Am. J. Enol. Vitic. 16 (1965), 144–153.
- [77] Hostettman, K.; Terreauv, C.; Marston, A.; Potteral, O. The role of planar chromatography in the rapid screening and isolation of bioactive compounds from medicinal plants. 9th International Symposium on Instrumental planar Chromatography, Interlaken, Switzerland, April 9-11, 1997.
- [78] Wongtong, S.; Tonsiripakdee, I.; Monhaphol, T.; Nonthabenja, R.; Pattanaargson-Wanichwecharrungruang, S. Post TLC developing technique for tyrosinase inhibitor detection. Biomed. Chrom. 21 (2007), 94-100.
- [79] Moure, A. ; Cruz, J.; Franco, D.; Dominguez, J.; Sineiro, J.; Dominguez, H.; Nunez, M.; Parajo, J. Natural antioxidants from agricultural sources. Food. Chem. 72 (2001), 145-171.

APPENDICES

APPENDIX A

A. Stock Solution Preparation

Phosphate buffer

Preparation of phosphate buffer stock solution 500 mM 1000 mL with K_2HPO_4 (MW 174.18, 42.5521 g) and KH_2PO_4 (MW 136.09, 34.7928 g) in deionizers water. K_2HPO_4 and KH_2PO_4 were dissolved in 900 mL deionizers water and measured pH with pH meter (pH 211 microprocessor pH meter, HANNA Instrument) then adjust pH to 6.8 with 0.1 M HCl and 0.1 M NaOH next adjust volume to 1000 mL.

$$pH = pK_a + \log \frac{[HPO_4^{2-}]}{[H_2PO_4^-]}$$

$$6.8 = 6.82 + \log \frac{[HPO_4^{2-}]}{[H_2PO_4^-]}$$

$$0.2 = \log \frac{[H_2PO_4^-]}{[HPO_4^{2-}]}$$

$$\frac{1.0471}{1} = \log \frac{[H_2PO_4^-]}{[HPO_4^{2-}]}$$

$$[H_2PO_4^-] = [CA]$$

$$[CA] = (1.0471/2.0471) \times 0.5$$

$$[CA] = 0.2557$$

KH_2HPO_4 was used 0.2557 moles, 34.7982 g

$$[HPO_4^{2-}] = [CB]$$

$$[CB] = (1/2.0471) \times 0.5$$

$$[CB] = 0.2443$$

K_2HPO_4 was used 0.2443 moles, 42.5521 g

APPENDIX B

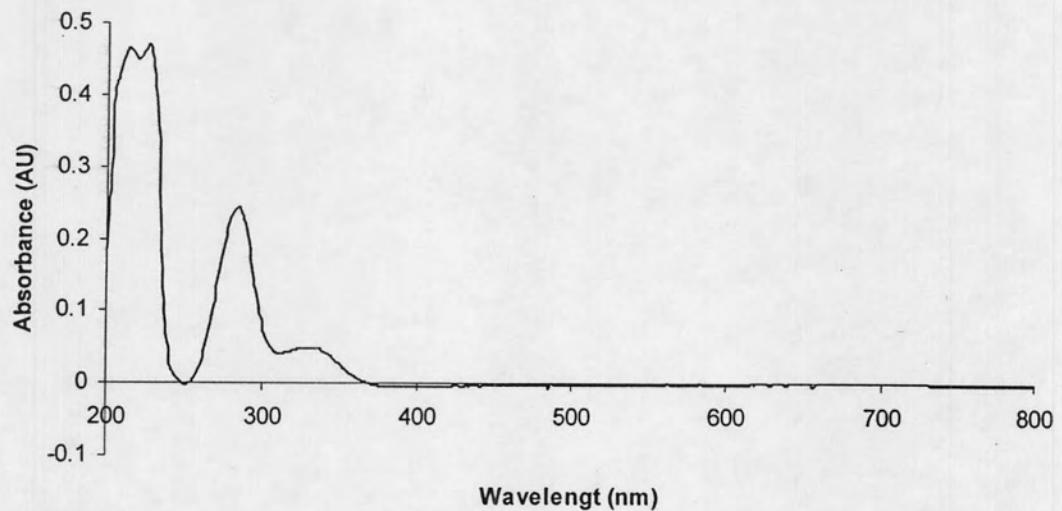


Figure B-1 UV Spectrum of naringin from KT albedo peels

APPENDIX C

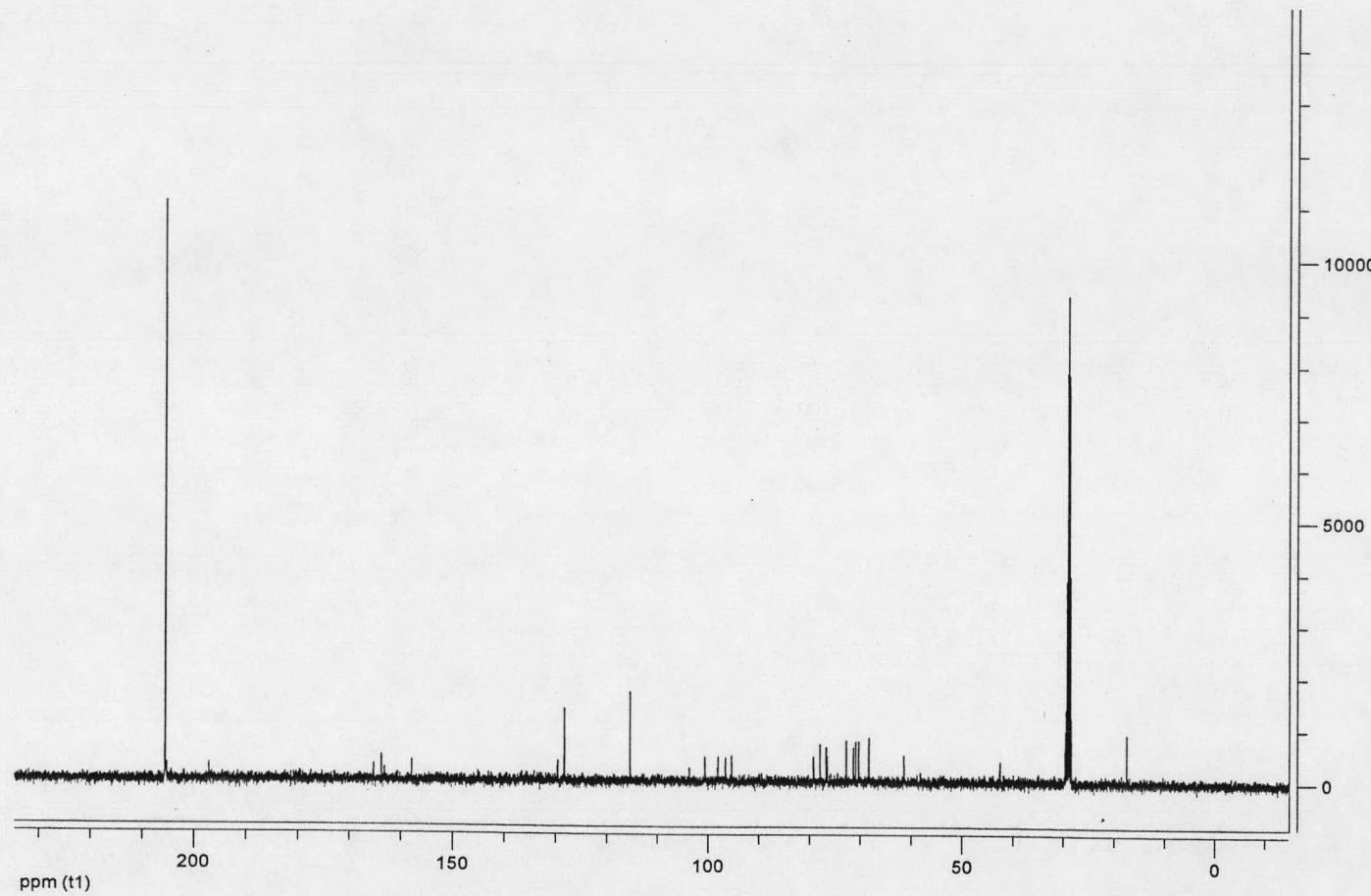


Figure C-1 The ^{13}C NMR spectrum (Acetone- d_6) of naringin

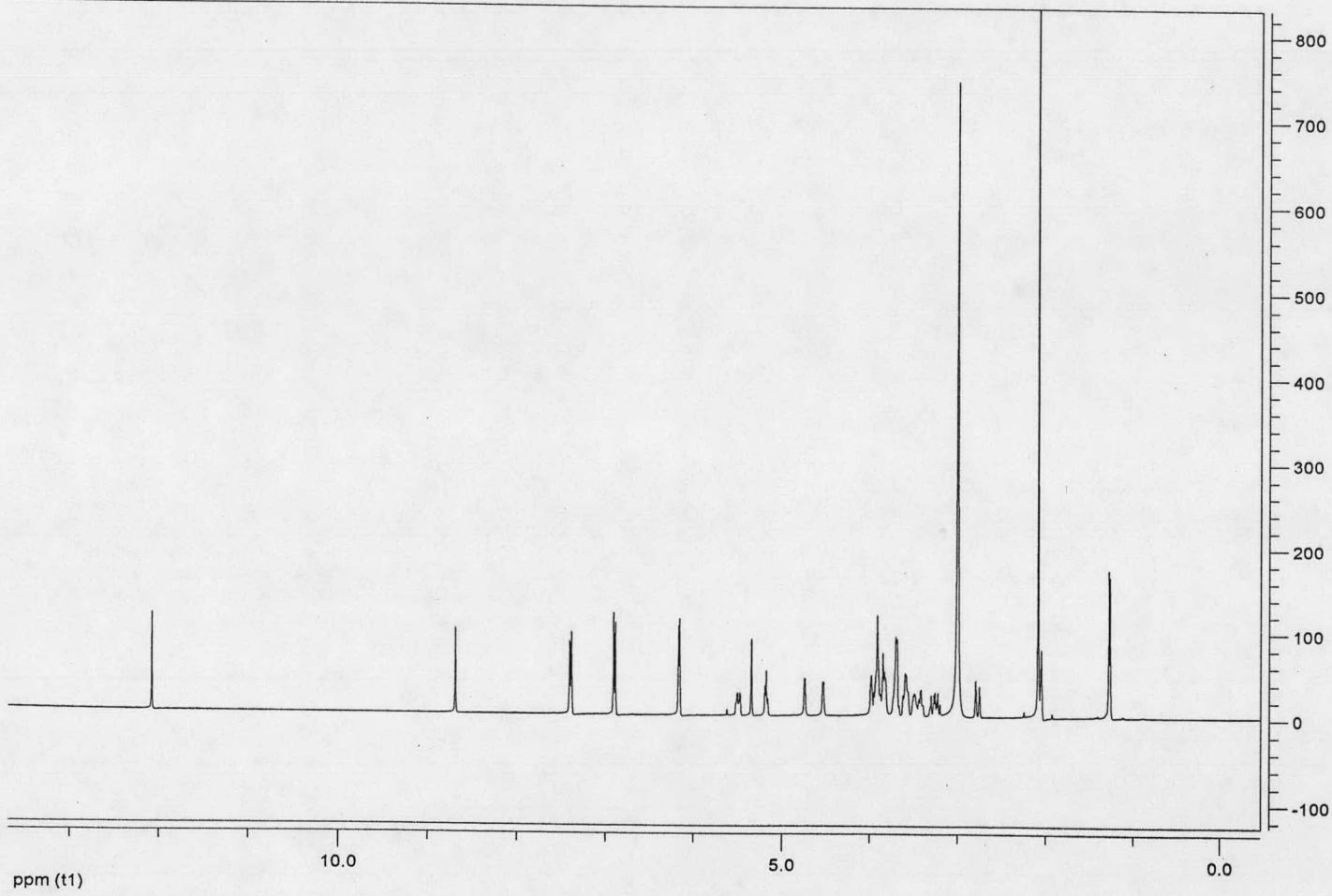


Figure C-2 The ${}^1\text{H}$ NMR spectrum (Acetone- d_6) of naringin

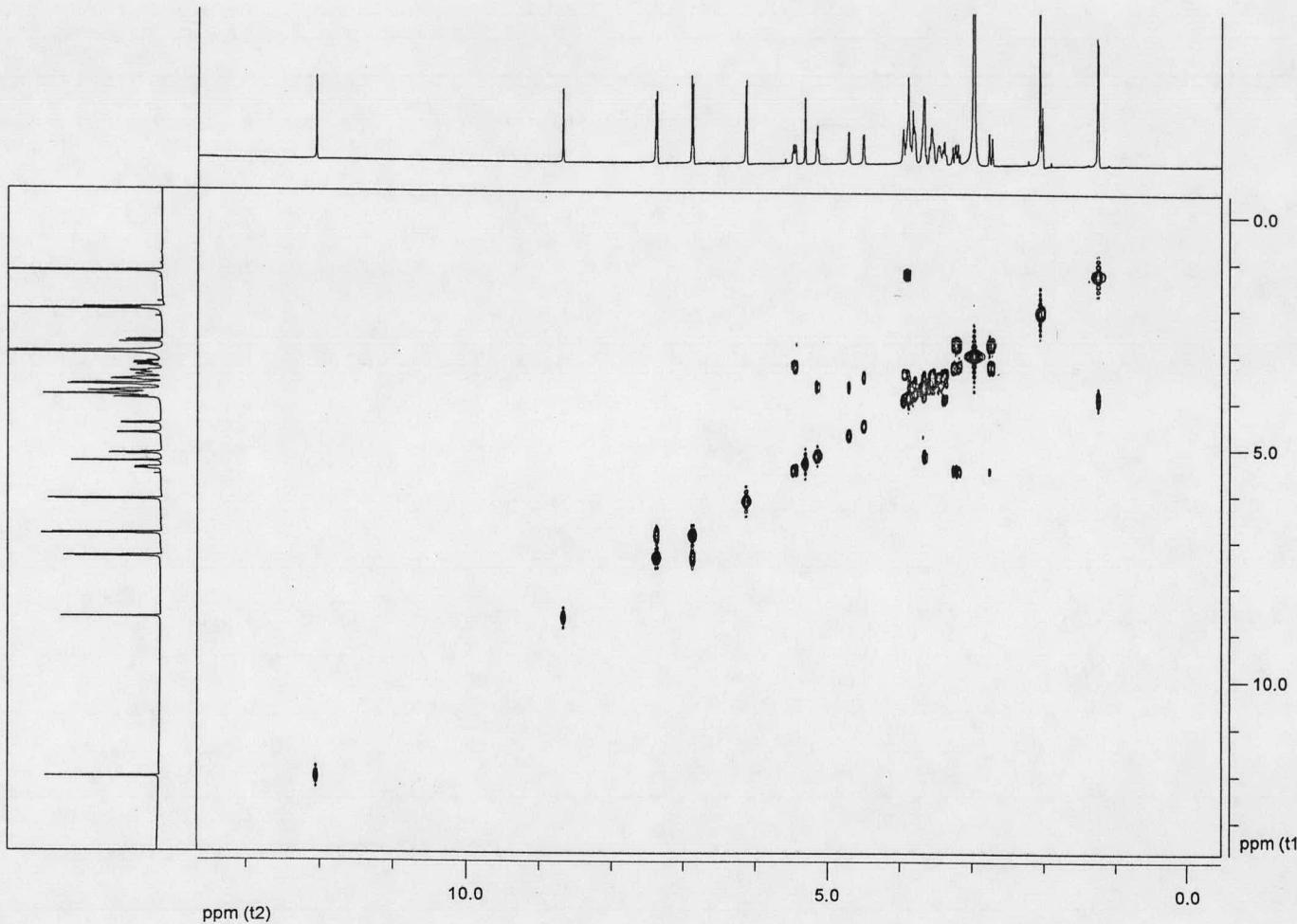


Figure C-3 The COSY spectrum ($\text{Acetone}-d_6$) of naringin

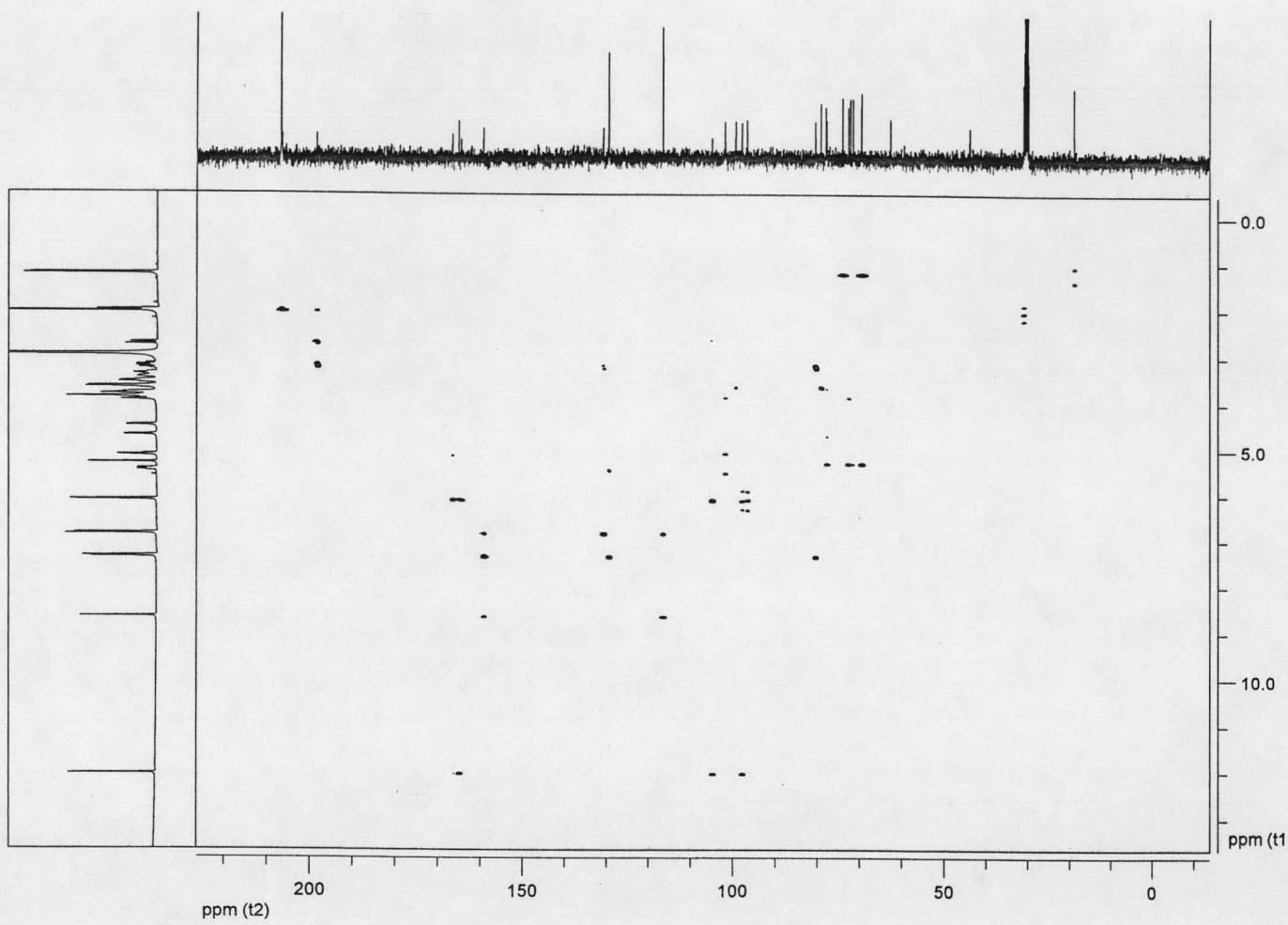


Figure C-4 HMBC spectrum (Acetone- d_6) of naringin

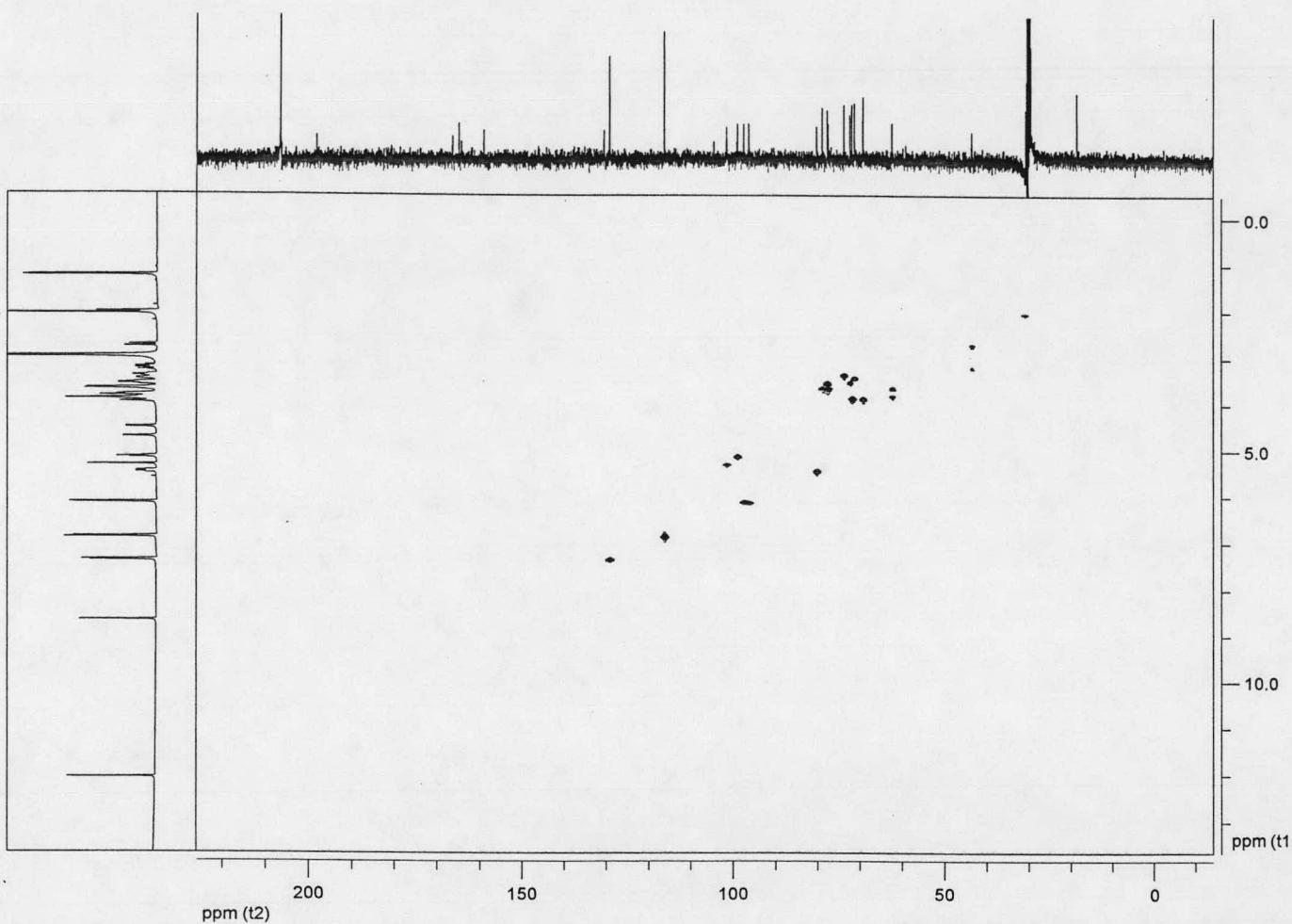


Figure C-5 HSQC spectrum (Acetone-*d*₆) of naringin

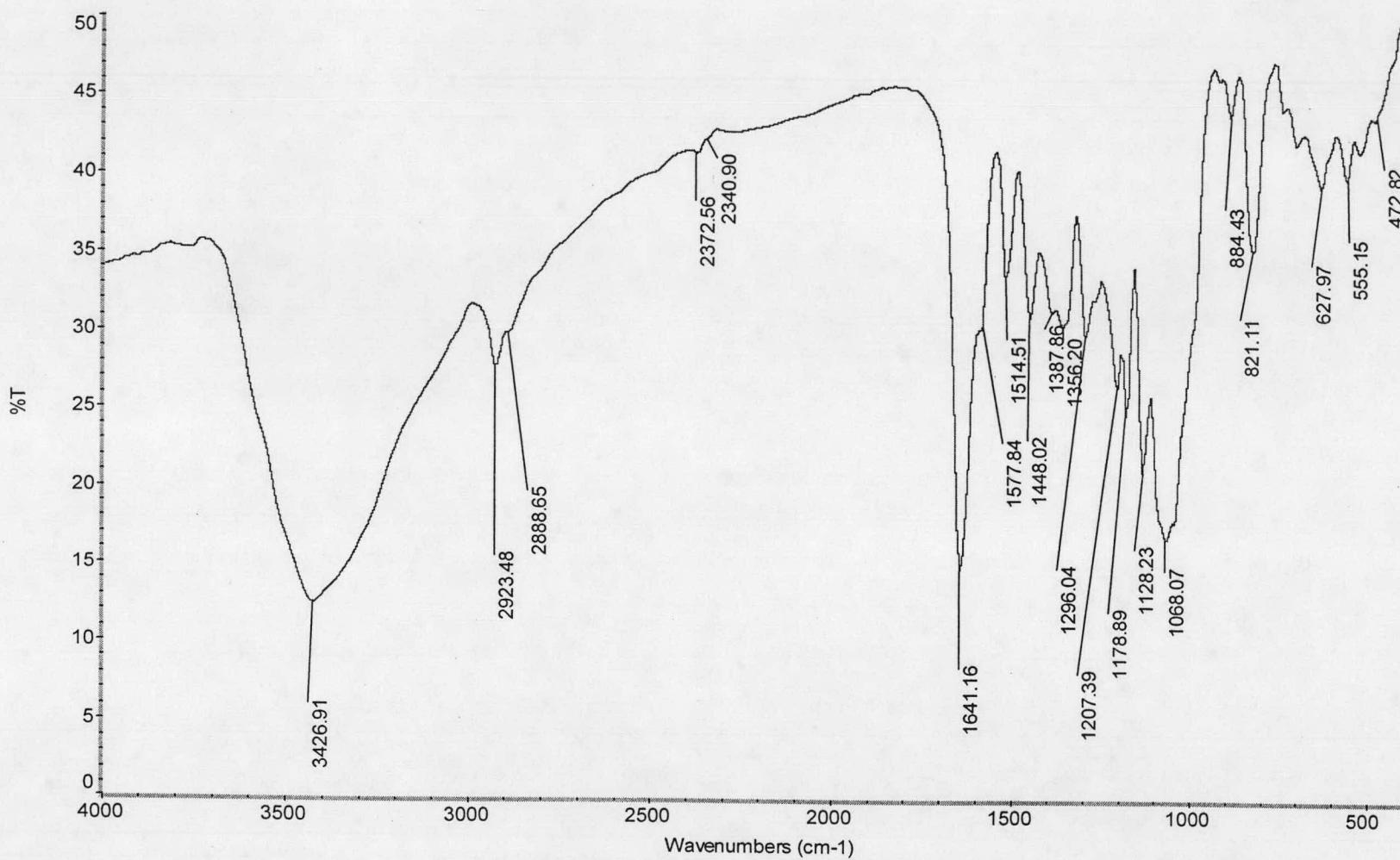


Figure C-6 The IR spectrum of naringin

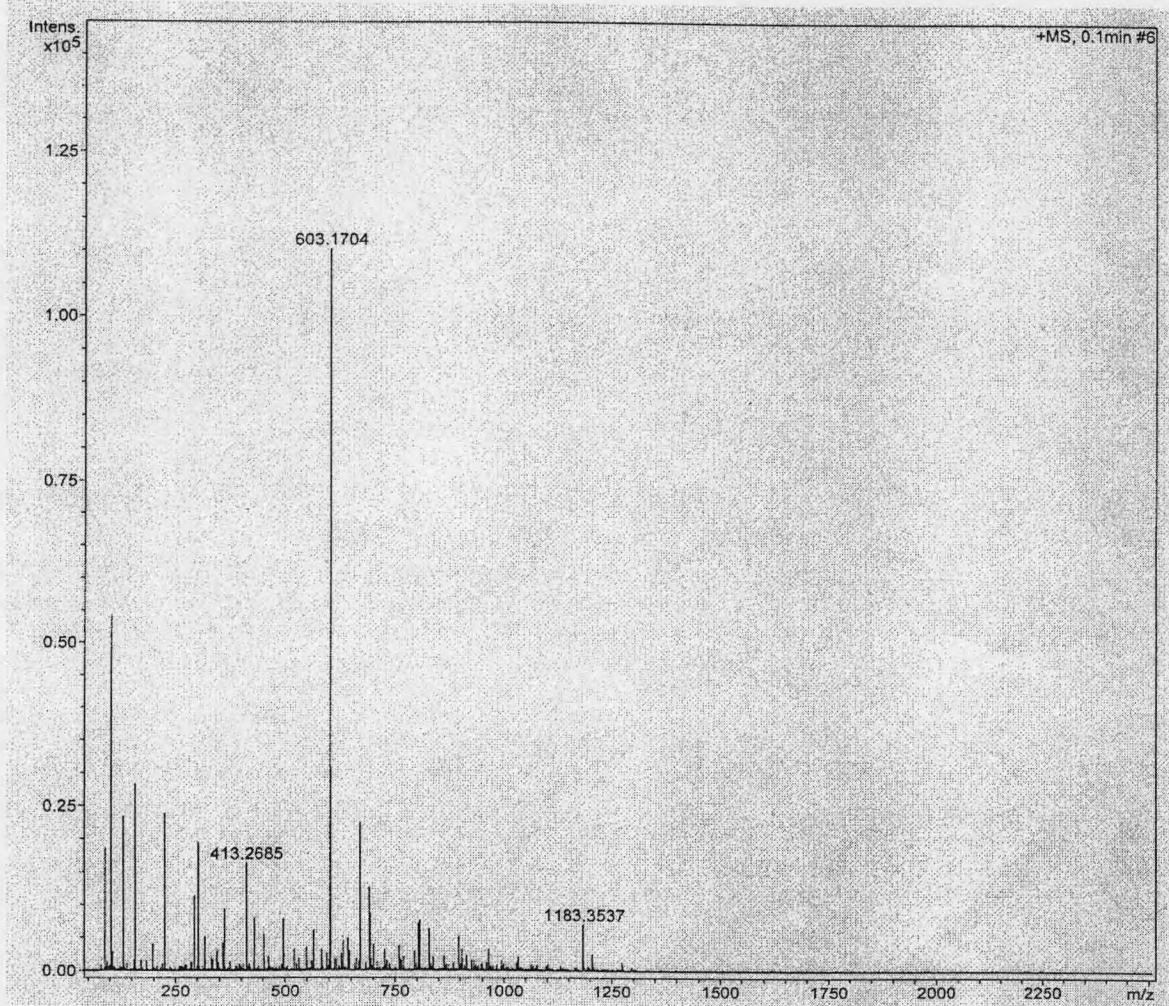


Figure C-7 The MS spectrum of naringin

VITA

Miss Kanokorn Sudto was born on 8th August, 1983 in Khon Kaen. She got a Bachelor of Science Degree in Biology from Kasetsart University in 2004. After that, Miss Kanokorn has been graduate student working for Master's Degree in Biotechnology program at Chulalongkorn University. During her Master of Science study, she was also awarded a research grant (Graduate School Thesis Grant) from Chulalongkorn University.

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