REFERENCES

1. **Introduction to the Fungi** [online] 2009 [cited 2009 December 21]. Available from: http://www.ucmp.berkeley.edu/fungi/fungi.html
2. **Fungi** [online] 2009 [cited 2009 December 22]. Available from: http://www.doctorfungus.org/thefungi/index.htm
3. **Mycology–Uses of Fungi–Fungal Drugs** [online] 2008 [cited 2008 April 12]. Availabl from:http://bugs.bio.usyd.edu.au/Mycology/UsesOf_Fungi/industrial Production/fungalDrugs.shtml
4. Gordon M, Cragg, David J. Newman. International in drug discovery and development from natural sources. **Pure Appl. Chem.** 2005; 77: 1923-1942.
5. Buss A.D. and Waigh R.D. Natural products as leads for new pharmaceuticals. **Burger's Medicinal Chemistry and Drug Discovery.** 1995; 1: 983-1033.
6. ***Chaetomium*** [online] 2009 [cited 2009 January 07] Available from: http://www.doctorfungus.org/thefungi/Chaetomium.htm
7. Brewer D, Jerram WA, Taylor A. The production of cochliodinol and a related metabolite by *Chaetomium* species. **Can. J. Microbiol.** 1968; 14: 861-866.
8. Safe S, Taylor A. Sporidesmins. Part XIII. Ovine III-thrift in Nova Scotia. Part III. The characterisation of chetomin a toxic metabolite of *Chaetomium cochliodes* and *Chaetomium globosum*. **J. Chem. Soc. Perkin I**. 1972; 472–479.
9. Takahashi M, Koyama K, Natori S. Four new azaphilones from *Chaetomium globosum* var. *flavo-viridae*. **Chem. Pharm. Bull.** 1990; 38(3): 625-628.
10. Kanokmedhakul S, Kanokmedhakul K, Nasomjai P, Louangsysouphanh S, Soytong K, Isobe M, et al. Antifungal azaphilones from the fungus *Chaetomium cupreum* CC3003. **J. Nat. Prod.** 2006; 69: 891-895.
11. Kanokmedhakul S, Kanokmedhakul K, Phonkerd N, Soytong K, Kongsaeree P, Suksamrarn A. Antimycobacterial anthraquinone-chromanone compound and diketopiperazine alkaloid from the fungus *Chaetomium globosum* KMITL-N0802. **Planta Med.** 2002; 68: 834-836.

12. Bashyal BP, Wijeratne EMK, Faeth SH, Gunatilaka AAL. Globosumones A-C, cytotoxic orsellinic acid esters from the Sonoran Desert endophytic fungus *Chaetomium globosum*. **J. Nat. Prod.** 2005; 68(5): 724-728.

13. Sekita S. Isocochliodinol and neocochliodinol, bis(3-indolyl)-benzoquinones from *Chaetomium* spp. **Chem. Pharm. Bull.** 1983; 31(9): 2998-3001.

14. Okeke B, Seiglemurandi F, Steiman R, Benoitguyod J, Kaouaji M. Identification of mycotoxin-producing fungal strains-A step in the isolation of compounds active against rice fungal disease. **J. Agr. Food Chem.** 1993; 41(10): 1731-1735.

15. Hwang EI, Yun BS, Kim YK, Kwon BM, Kim HG, Lee HB, et al. Chaetoatrosin A, a novel chitin synthase II inhibitor produced by *Chaetomium atrobrunneum* F449. **J. Antibiot.** 2000; 53(3): 248-255.

16. Oh H, Swenson DC, Gloer JB, Wicklow DT, Dowd PF. Chaetochalasin A: a new bioactive metabolite from *Chaetomium brasiliense*. **Tetrahedron Lett.** 1998; (39): 7633-7636.

17. Li GY, Li BG, Yang T, Liu GY, Zhang GL. Secondary metabolites from the fungus *Chaetomium brasiliense*. **Helv. Chim. Acta** 2008; 91: 124-129.

18. Khumkomkhet P, Kanokmedhakul S, Kanokmedhakul, Hahnvajanawong C, Soytong K. Antimalarial and Cytotoxic Depsidones from the Fungus *Chaetomium brasiliense*. **J. Nat. Prod.** 2009; 72: 1487-1491.

19. Wijeratne EMK, Paranagama PA, Gunatilaka AAL. Five new isocoumarins from Sonoran desert plant-associated fungal strains *Paraphaeosphaeria quadriseptata* and *Chaetomium chiversii*. **Tetrahedron** 2006; 62: 8439-8446.

20. Burrows BF, Turner WB, Walker ERH. 8-Ethylidene-7,8-dihydro-4-methoxypyrano[4,3-*b*]pyran-2,5-dione (Coarctatin), a metabolite of *Chaetomium coarctatum*. **J. Chem. Soc. Perkin I** 1975; 999-1000.

21. Seto H, Shibamiya M, Yonehara H. Utilization of ^{13}C-^{13}C coupling in structural and biosynthetic studies. XI. Biosynthetic studies of coarctatin. **J. Antibiot.** 1978; 31(9): 926-928.

22. Saito M, Seto H, Yonehara H. Biosynthesis of 2-(but-1,3-dienyl)-3-hydro-4-(penta-1,3-dienyl)-tetrahydrofuran, a metabolite of *Chaetomium coarctatum*. **Agric. Biol. Chem.** 1983; 47(12): 2935-2937.

23. Brewer D, Duncan JM, Jerram WA, Leach CK, Safe S, Taylor A, etal. Ovineill-thrift in Nova Scotia. 5.The production and toxicology of chetomin. A metabolite of *Chaetomium* spp. **Can. J. Microbiol.** 1972; 18: 1129-1137.

24. Abraham WR, Arfmann HA. Rearranged tetrahydrofurans from *Chaetomium cochlioides*. **Phytochemistry** 1992; 31(7): 2405-2408.

25. Kang JG, Kim KK, Kang KY. Antaginism and structural identification of antifungal compound from *Chetomium cochliodes* against phytopathogenic fungi. **Agric. Chem. Biotechnol.** 1999; 42(3): 146-150.

26. Li GY, Li BG, Yang T, Yan JF, Liu GY, Zhang GL. Chaetocochins A-C, epipolythiodioxopiperazines from *Chaetomium cochliodes*. **J. Nat. Prod.** 2006; 69: 1374-1376.

27. Phonkerd N, Kanokmedhakul S, Kanokmedhakul K, Soytong K, Prabpai S, Kongsearee P. Bis-spiro-azaphilones and azaphilones from the fungi *Chaetomium cochliodes* VTh01 and C. cochliodes CTh05. **Tetrahedron.** 2008; 64(40): 9636-9645.

28. Payne DJ, et al. Identification of a series of tricyclic natural products as potent broad-spectrum inhibitors of metallo-β-lactamases. **Antimicrob Agents Chemother** 2002; 46(6): 1880-1886.

29. Brewer D, Duncan JM, Jerram WA, Leach CK, Safe S, Taylor A, et al. Ovine ill-thrift in Nova Scotia. 5. The production and toxicology of chetomin, a metabolite of *Chaetomium* spp. **Can. J. Microbiol.** 1972; 18: 1129-1137.

30. Sekita S, Yoshihira K, Natori S. Structures of chaetoglobosin A and B, cytotoxic metabolites of *Chaetomium globosum*. **Tetrahedron Lett.** 1973; (23): 2109-2112.

31. Sekita S, Yoshihira K, Natori S. Structures of chaetoglobosin C, D, E and F, cytotoxic indol-3-yl-[13] cytochalasans from *Chaetomium globosum*. **Tetrahedron Lett.** 1976; (17): 1351-1354.

32. Sekita S, Yoshihira K, Natori S. Chaetoglobosins G and J, cytotoxic indol-3-yl[13]-cytochalasans from *Chaetomium globosum*. **Tetrahedron Lett.** 1977; (32): 2771-2774.

33. Itoh Y, Kodama K, Furuya K, Takahashi S, Haneishi T, Takiguchi Y, et al. A new sesquiterpene antibiotic, heptelidic acid producing organisms, fermentation, isolation and characterization. **J. Antibiot.** 1980; 33(5): 468-473.

34. Itoh Y, Takahashi S, Haneishi T, Arai M. Structure of heptelidic acid, a new sesquiterpene antibiotic from fungi. **J. Antibiot.** 1980; 33(5): 525-526.

35. Kikuchi T, Kodata S, Nakamura K, Nishi A, Taga T, Kaji T, et al. Dethio-tetra (methylthio) chetomin, a new antimicrobial metabolite of *Chaetomium globosum* KINZE EX FR. structure and partial synthesis from chetomin. **Chem. Pharm. Bull.** 1982; 30(10): 3846-3848.

36. Sekita S, Yoshihira K, Natori S, Udagawa SI, Sakabe F, Kurata H, et al. Chaetoglobisins, cytotoxicity 10-(indol-3-yl)-[13] cytochalasans from *Chaetomium spp.* I. Production, Isolation and some cytological effects of chaetoglobosins A-J. **Chem. Pharm. Bull.** 1982; 30(5): 1609-1617.

37. Sekita S, Yoshihira K, Natori S. Chaetoglobosins, cytotoxic 10-(indol-3-yl)-[13]cytochalasans from *Chaetomium* spp. IV. ^{13}C-nuclear magnetic resonance spectra and their application to a biosynthetic study. **Chem. Pharm. Bull.** 1983; 31(2): 490-498.

38. Di Pietro A, Gut-Rella M, Pachlatko JP, Schwinn FJ. Role of antibiotics produced by *Chaetomium globosum* in biocontrol of *Pythium ultimum*, a causal agent of damping-off. **Phytopathology** 1992; 82(2): 131-135.

39. Breinholt J, Demuth H, Heide M, Jensen G, Moller I, Nielsen R, et al. Prenisatin (5-(3-methyl-2-butenyl)-indole-2,3-dione) an antifungal isatin derivative from *Chaetomium globosum*. **Acta Chem. Scand** 1996; 50(5): 443-445.

40. Tabata Y, Miiko N, Yaguchi T, Hatsu M, Ishii S, Imai S. PF1138A and B, novel trans-epoxysuccinate-type cysteine protease inhibitors produced by *Chaetomium globosum*. **Meiji Seika Kenkyu Nenpo** 2000; 39: 55-64.

41. Jiao W, Feng Y, Blunt JW, Cole ALJ, Munro MHG. Chaetoglobosins Q, R, and T, three further new metabolites from *Chaetomium globosum*. **J. Nat. Prod.** 2004; 67(10): 1722-1725.

42. Ding G, Song YC, Chen JR, Xu C, Ge HM, Wang XT, et al. Chaetoglobosin U, a cytochalasan alkaloid from endophytic *Chaetomium globosum* IFB-E019. **J. Nat. Prod.** 2006; 69: 302-304.

43. Wijeratne EMK, Turbyville TJ, Fritz A, Whitesell L, Gunatilaka AAL. A new dihydroxanthenone from a plant-associated strain of the fungus *Chaetomium globosum* demonstrates anticancer activity. **Bioorg. Med. Chem.** 2006; 14: 7917-7923.

44. Wang S, Li XM, Teuscher F, Li DL, Diesel A, Ebel R, et al. Chaetopyranin, a benzaldehyde derivative, and other related metabolites from *Chaetomium globosum*, an endophytic fungus derived from the marine red alga *Polysiphonia urceolata*. **J. Nat. Prod.** 2006; 69(11): 1622-1625.

45. Yang SW, Mierzwa R, Terrcciano J, Patel M, Gullo V, Wagner N, et al. Chemokine receptor CCR-5 inhibitors produced by *Chaetomium globosum*. **J. Nat. Prod.** 2006; 69: 1025-1028.

46. Wang S, Zhang Y, Li XM, Wang BG. Benzaldehydes from endophytic fungus *Chaetomium globosum* separated from marine red alga *Polysiphonia urceolata*. **Haiyang Yu Huzhao** 2007; 38(2): 131-135.

47. Yang SW, Mierzwa R, Terracciano J, Patel M, Gullo V, Wagner N, et al. Sch 213766, a novel chemokine receptor CCR-5 inhibitor from *Chaetomium globosum*. **J. Antibiot.** 2007; 60(8): 524-528.

48. Yamada T, Doi M, Shigeta H, Muroga Y, Hosoe S, Numata A, et al. Absolute stereostructures of cytotoxic metabolites, chaetomugilins A-C, produced by *Chaetomium* species separated from a marine fish. **Tetrahedron Lett.** 2008; (49): 4192-4195.

49. Matthew R, David R, Cynthia A, David C. Growth and Mycotoxin Production by *Chaetomium globosum* Is Favored in a Neutral pH. **Int. J. Mol. Sci**. 2008; 9: 2357-2365.

50. Hui MG, Wei YZ, Gang D, Saparpakorn P, Yong CS, Supa H, Ren XT. Chaetoglobins A and B, two unusual alkaloids from endophytic *Chaetomium globosum* culture. **Chem. Commun.** 2008; 5978-5980.

51. Yasuhide M, Yamada T, Numata A, Tanaka R. Chaetomugilins, New Selectively Cytotoxic Metabolites, Produced by a Marine Fish-derived *Chaetomium Species*. **J. Antibiot.** 2008; 61(10): 615-622.

52. Yamada T, Yasuhide M, Shigeta H, Numata A, Tanaka R. Absolute stereostructures of chaetomugilins G and H produced by a marine-fish-derived *Chaetomium* species. **J. Antibiot.** 2009; 62: 353-357.

53. Muroga Y, Yamada T, Numata A, Tanaka R. Chaetomugilins I-O, new potent cytotoxic metabolites from a marine-fish-derived *Chaetomium* species. Stereochemistry and biological activities. **Tetrahedron.** 2009, 65: 7580-7586.

54. Qin JC, Gao JM, Zhang YM. Yang SX, Bai MS, Ma YT, Laatsch H. Polyhydroxylated steroids from an endophytic fungus, *Chaetomium globosum* ZY-22 isolated from *Ginkgo bioba*. **Steroids.** 2009; 74: 786-790.

55. Yamada T, Muroga Y, Tanaka R. New Azaphilones, *Seco*-Chaetomugilins A and D, Produced by a Marine-Fish-Derived *Chaetomium globosum*. **Mar.Drugs.** 2009 , 7: 249-257.

56. Koyama K, Natori S. Chaetochromins B, C, and D; bis(naphtho-γ-pyrone) derivatives from *Chaetomium gracile*. **Chem. Pharm. Bull.** 1987; 35(2): 578-584.

57. Koyama K, Natori S, Biosynthesis of chaetochromin A, a bis(naphtha-γ-pyrone), in Chaetomium spp. **Chem. Pharm. Bull**. 1989; 37(8): 2022-2025.

58. Li GY, Li BG, Yang T, Liu GY, Zhang GL. Chaetoindicins A-C, three isoquinoline alkaloids from the fungus *Chaetomium indicum*. **Org. Lett**. 2006; 8(16): 3613-3615.

59. Stark AA, Kobbe B, Matsuo K, Buchi G, Wogan GN, Demain AL. Mollicellins: mutagenic and antibacterial mycotoxins. **Appl. Environ. Microbiol.** 1978; 36: 412-420. 49.

60. Sekita S. Isocochliodinol and neocochliodinol, bis(3-indolyl)-benzoquinones from *Chaetomium* spp. **Chem. Pharm. Bull.** 1983; 31(9): 2998-3001.

61. Saito T, Suzuki Y, Koyama K, Natori S, Iitaka Y, Kinoshita T. Chetracin A and chaetocins B and C, three new epipolythiodioxopiperazines from *Chaetomium* spp. **Chem. Pharm. Bull.** 1988; 36(6): 1942-1956.

61. Saito T, Suzuki Y, Koyama K, Natori S, Iitaka Y, Kinoshita T. Chetracin A and chaetocins B and C, three new epipolythiodioxopiperazines from *Chaetomium* spp. **Chem. Pharm. Bull.** 1988; 36(6): 1942-1956.

62. Smetanina OF, Denisenko VA, Pivkin MV, Khudyakova YV, Gerasimenko AV, Popov DY, et al. 3β-methoxyolean-18-ene (miliacin) from the marine fungus *Chaetomium olivaceum*. **Russ. Chem. Bull.** 2001; 50(12): 2463-2465.

63. Fujimoto H, Nozawa M, Okuyama E, Ishibashi M. Five new chromones possessing monoamine oxidase inhibitory activity from an ascomycete, *Chaetomium quadrangulatum*. **Chem. Pharm. Bull.** 2002; 50(3): 330-336.

64. Fujimoto H, Nozawa M, Okuyama E, Ishibashi M. Six new constituents from an ascomycete, *Chaetomium quadrangulatum*, found in a screening study focused on monoamine oxidase inhibitory activity. **Chem. Pharm. Bull.** 2003; 51(3): 247-251.

65. Fujimoto H, Sumino M, Okuyama E, Ishibashi M. Immunomodulatory constituents from an ascomycete, *Chaetomium seminudum*. **J. Nat. Prod.** 2004; 67(1): 98-102.

66. Oikawa H, Murakami Y, Ichihara A. 20-Ketoreductase activity of chaetoglobosin A and prochaetoglobosins in a cell-free system of *Chaetomium subaffine* and the isolation of new chaetoglobosins. **Biosci. Biotechnol. Biochem.** 1993; 57(4): 628-631.

67. Rether J, Erkel G, Anke T, Sterner O. Oxaspirodion, a new inhibitor of inducible TNF-α expression from the Ascomycete *Chaetomium subspirale*. Production, isolation and structure elucidation. **J. Antibiot.** 2004; 57(8): 493-495.

68. Sekita S, Yoshihira K, Natori S. Chaetochromin, a bis(naphthodihydropyran-4-one) mycotoxin from *Chaetomium thielavioideum*: application of ^{13}C-^{1}H long-rang coupling to the structure elucididation. **Chem. Pharm. Bull.** 1980; 28(8): 2428-2435.

69. Cole RJ, Kirksey JW, Cutler HG, Davis EE. Toxic effects of oosporein from *Chaetomium trilaterale*. **J. Agr. Food Chem.** 1974; 22(3): 517-520.

70. Lösgen S, Schlörke O, Meindl K, Herbst-Irmer R, Zeeck A. Structure and biosynthesis of chaetocyclinones, new polyketides produced by an endosymbiotic fungus. **Eur. J. Org. Chem.** 2007; (13): 2191-2196.

71. Marwah RG, Fatope MO, Deadman ML, Al-Maqbali YM, Husband J. Musanahol: a new aureonitol-related metabolite from a *Chaetomium* sp. **Tetrahedron.** 2007; 63(34): 8174-8180.

72. Ahmed AL. Chaetominedione, a new tyrosine kinase inhibitor isolated from the algicolous marine fungus *Chaetomium sp.* **Tetrahedron Lett.** 2008; 49: 6398-6400.

73. Pouchert, C. J.; Behnke, J. Ergosterol. **The Aldrich Library of ^{13}C and ^{1}H NMR Spectra. 1st ed.** USA: Aldrich Chemical Co.; 1993.

74. Jinming G, Lin H, Jikai L. A novel sterol from Chinese truffles *Tuber indicum.* **Steroids** 2001; 66: 771-775.

75. Zhou X, Song B, Jin L, Hu D, Diao C, Xu G, et al. Isolation and inhibitory activity against ERK phosphorylation of hydroxyanthraquinones from rhubarb. **Bioorg. Med. Chem. Lett.** 2006; 16: 563–568.

76. Trager W, Jensen JB. Human malaria parasites in continuous culture. **Science** 1976; 193: 673-675.

77. Desjardins RE, Canfield CJ, Haynes JD, Chulay JD. Quantitative assessment of antimalarial activity in vitro by a semiautomated microdilution technique. **Antimicrob Agents and Chemother** 1979; 16(6): 710-718.

78. Collins LA, Franzblau SG. Microplate Alamar blue assay versus BACTEC 460 system for high-throughput screening of compounds against *Mycobacterium tuberculosis* and *Mycobacterium avium.* **Antimicrob Agents and Chemother** 1997; 41(5): 1004-1009.

79. Scudiero, D. A.; Shoemaker, R. H.; Paull, K. D.; Monka, A.; Tierney,S.; Nofziger, T. H.; Currens, M. J.; Seniff, D.; Boyd, M. R. Evaluation of a Soluble Tetrazolium/Formazan Assay for Cell Growth and Drug Sensitivity in Culture Using Human and Other Tumor Cell Lines. **Cancer Res.** 1988, 48, 4827–4833.

81. Ingerman-Wojenski, C.M., Silver M.J. A quick method for screening platelet dysfunctions using the whole blood lumi-aggregometer. **Thromb. Haemostasis.** 1984, 2: 154-156.

82. Challen, A., Branch, W.J., Cummings, J.H. Quantitation of platelet mass during aggregation in the electronic (Wellcome) whole blood aggregometer. **J. Pharmacol.** 1982, 8: 115-122.

83. Dong, H., Chen, S-X. Anew antiplatelet diarylheptanoid from *Alpinia blepharocalyx*. **J. Nat. Prod.** 1998; 61: 142-144.

APPENDIX

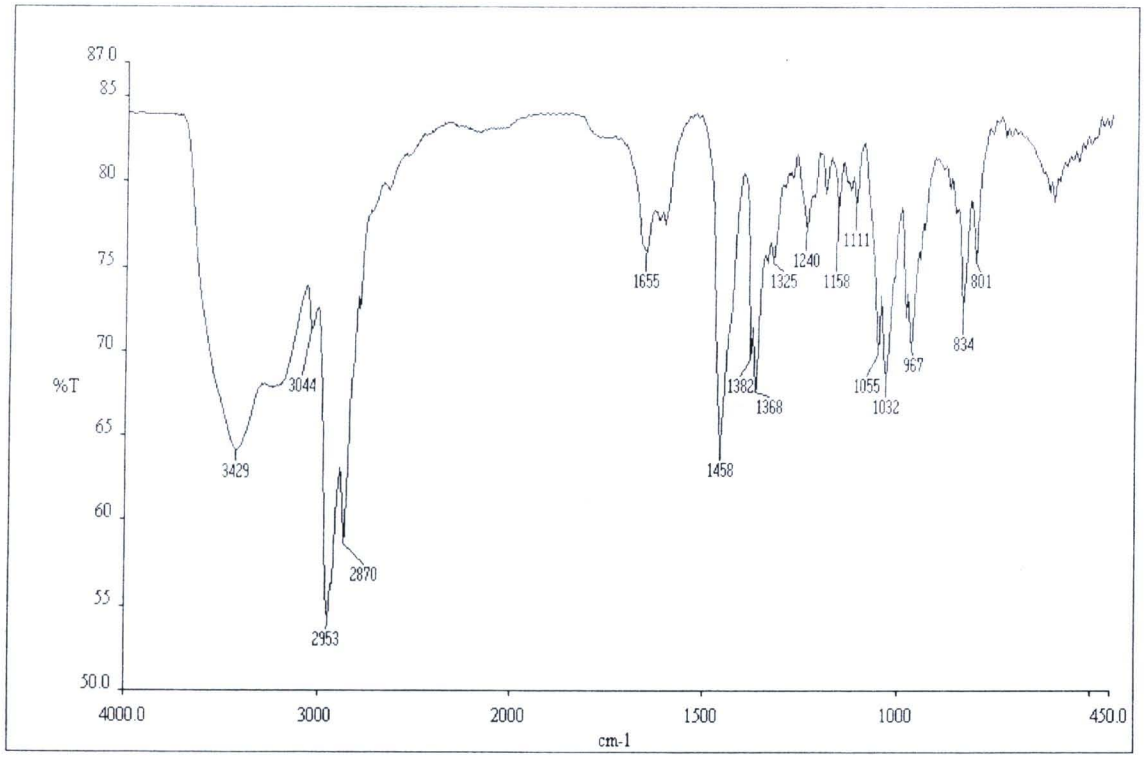

Figure 1 IR spectrum of ergosterol (**1.1, 2.1** or **3.1**).

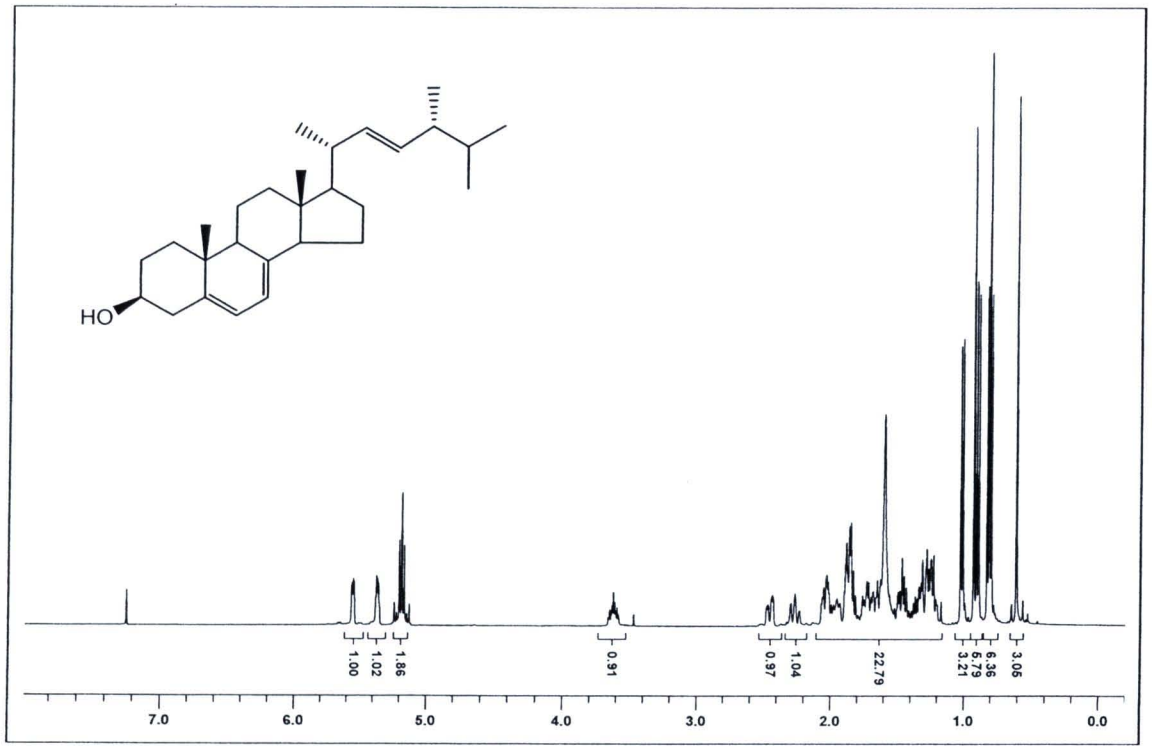

Figure 2 ^{1}H NMR spectrum of ergosterol (**1.1, 2.1** or **3.1**).

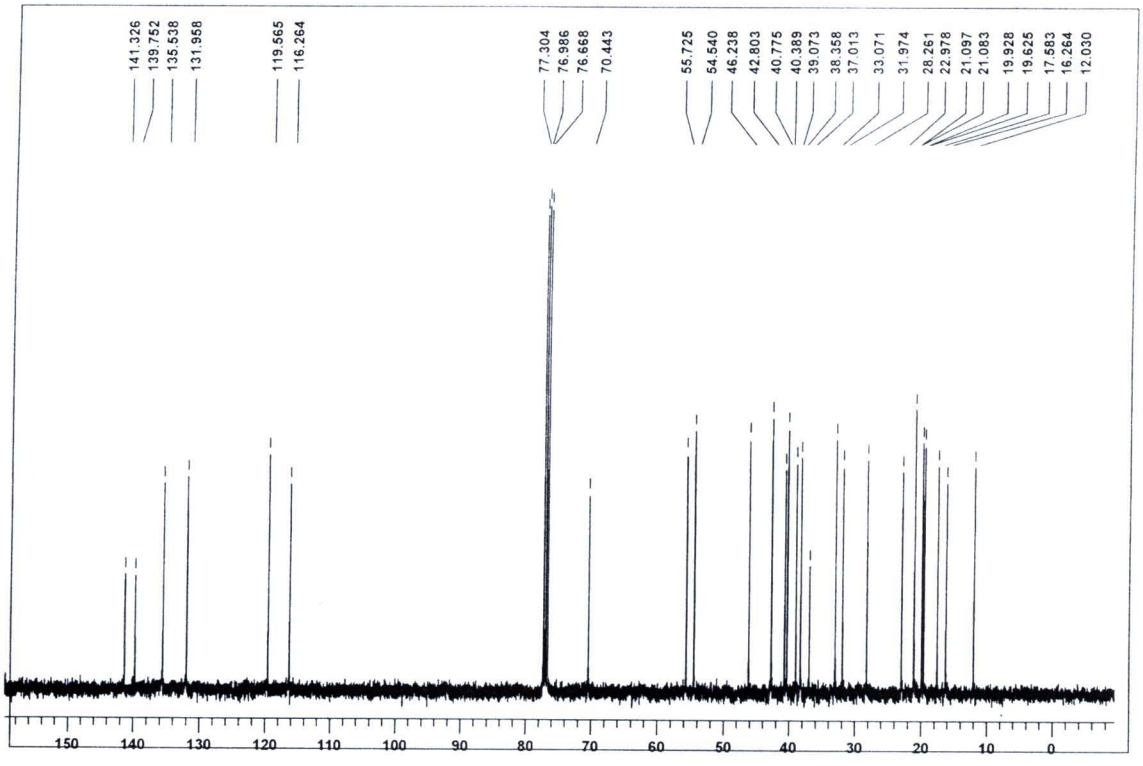

Figure 3 ^{13}C NMR spectrum of ergosterol (**1.1, 2.1** or **3.1**).

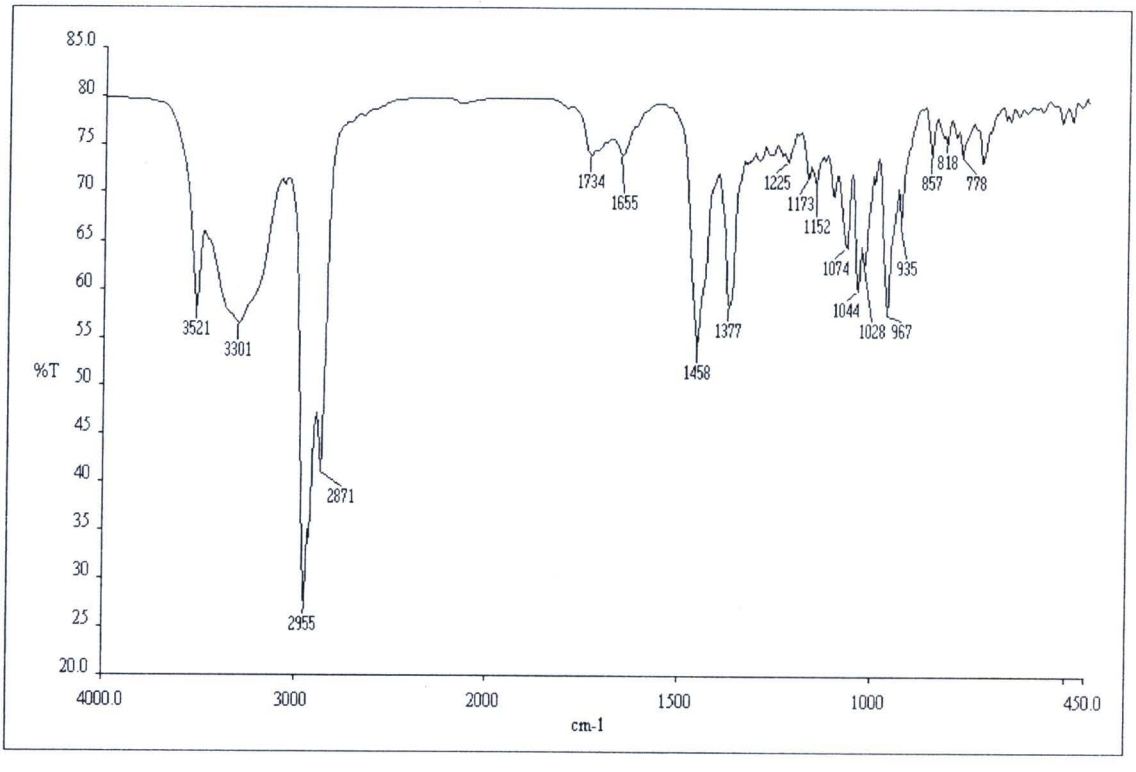

Figure 4 IR spectrum of ergosterol peroxide (**1.2, 2.2 or 3.2**).

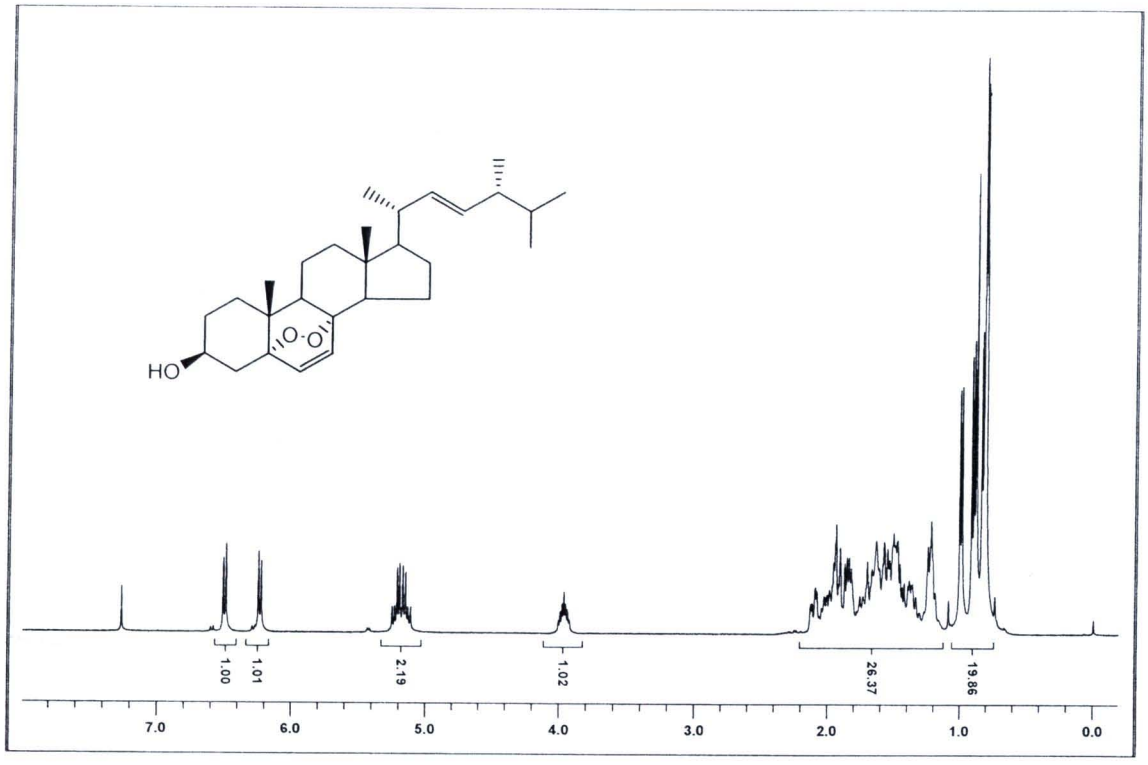

Figure 5 ^{1}H NMR spectrum of ergosterol peroxide (**1.2, 2.2 or 3.2**).

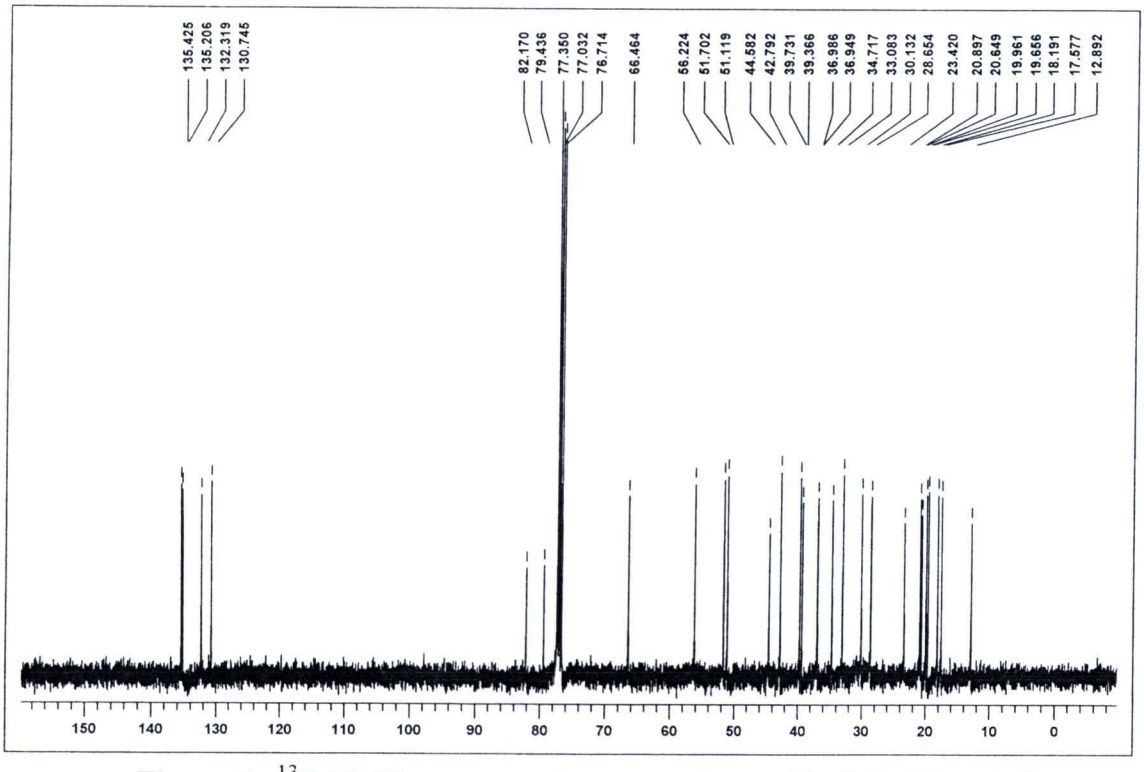

Figure 6 ^{13}C NMR spectrum of ergosterol peroxide (**1.2, 2.2 or 3.2**).

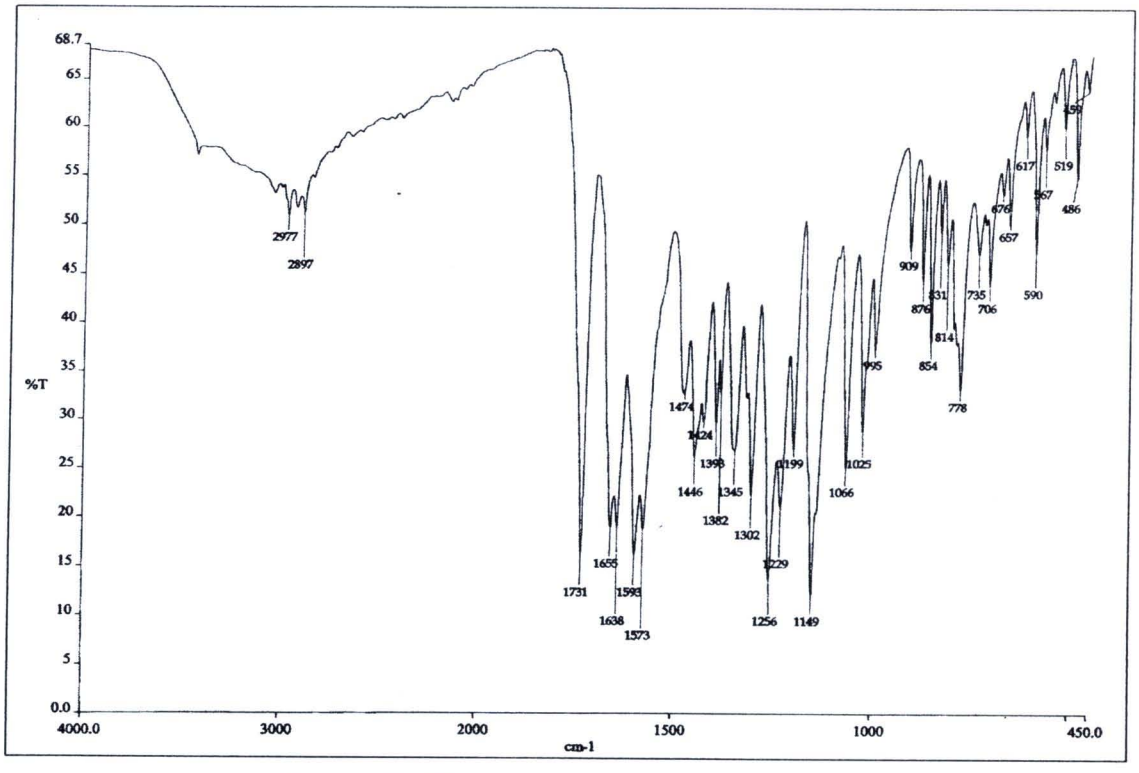

Figure 7 IR spectrum of mollicellin H (**1.3**).

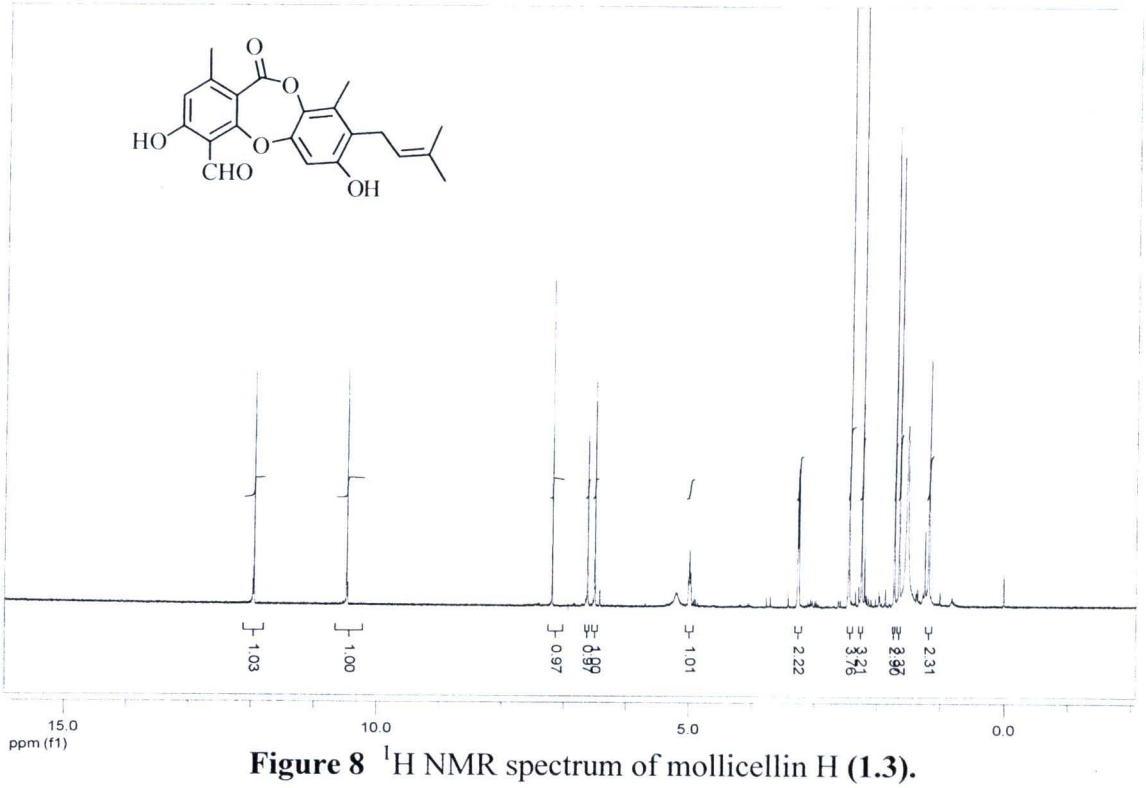

Figure 8 ^{1}H NMR spectrum of mollicellin H **(1.3).**

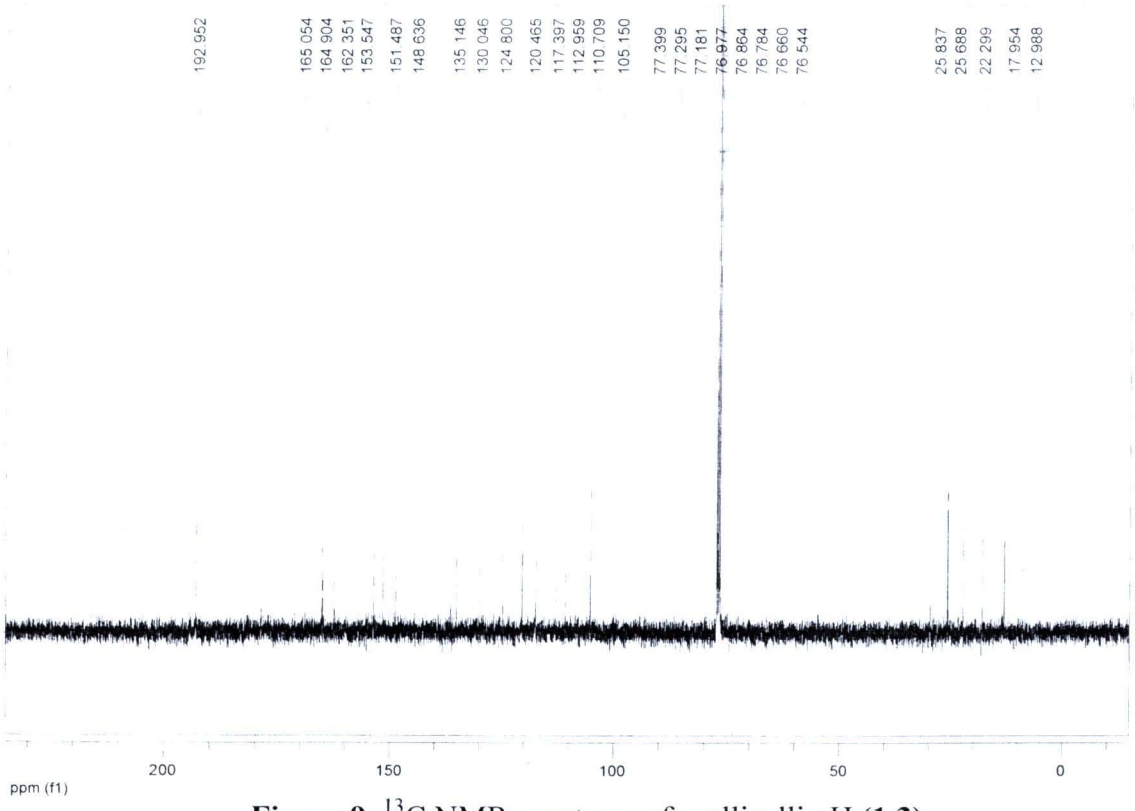

Figure 9 ^{13}C NMR spectrum of mollicellin H **(1.3).**

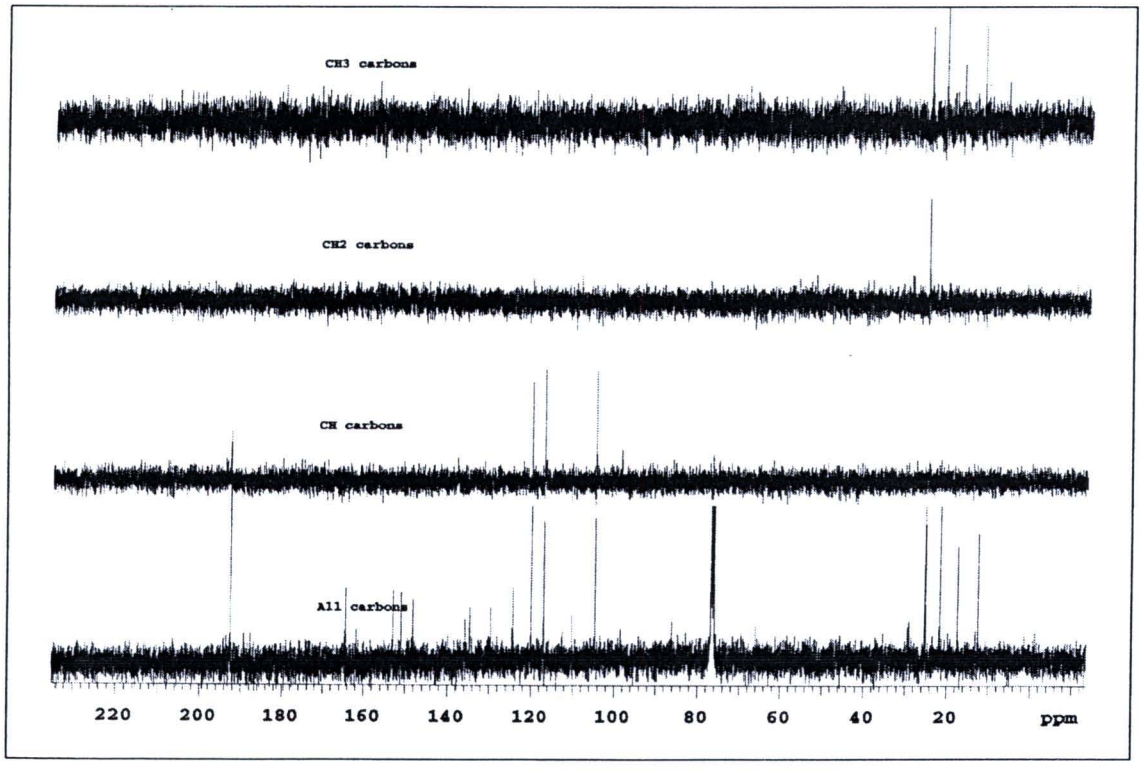

Figure 10 DEPT spectrum of mollicellin H **(1.3).**

Figure 11 HSQC spectrum of mollicellin H **(1.3)**.

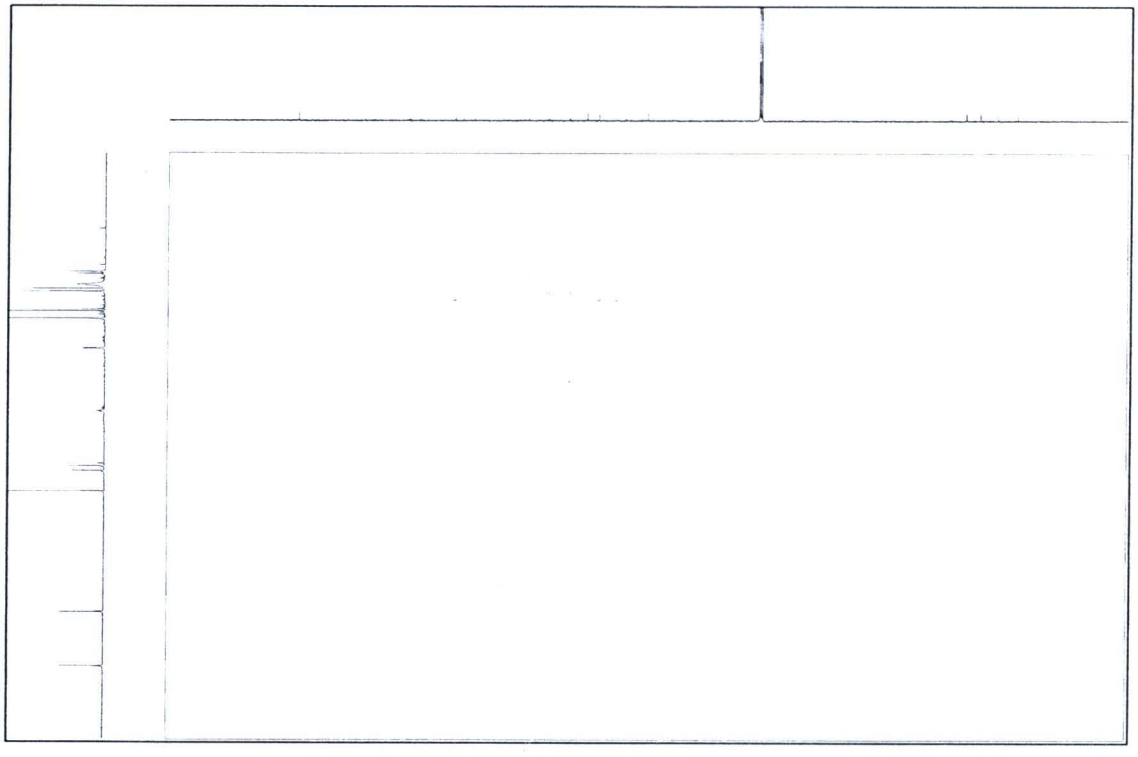

Figure 12 HMBC spectrum of mollicellin H **(1.3)**.

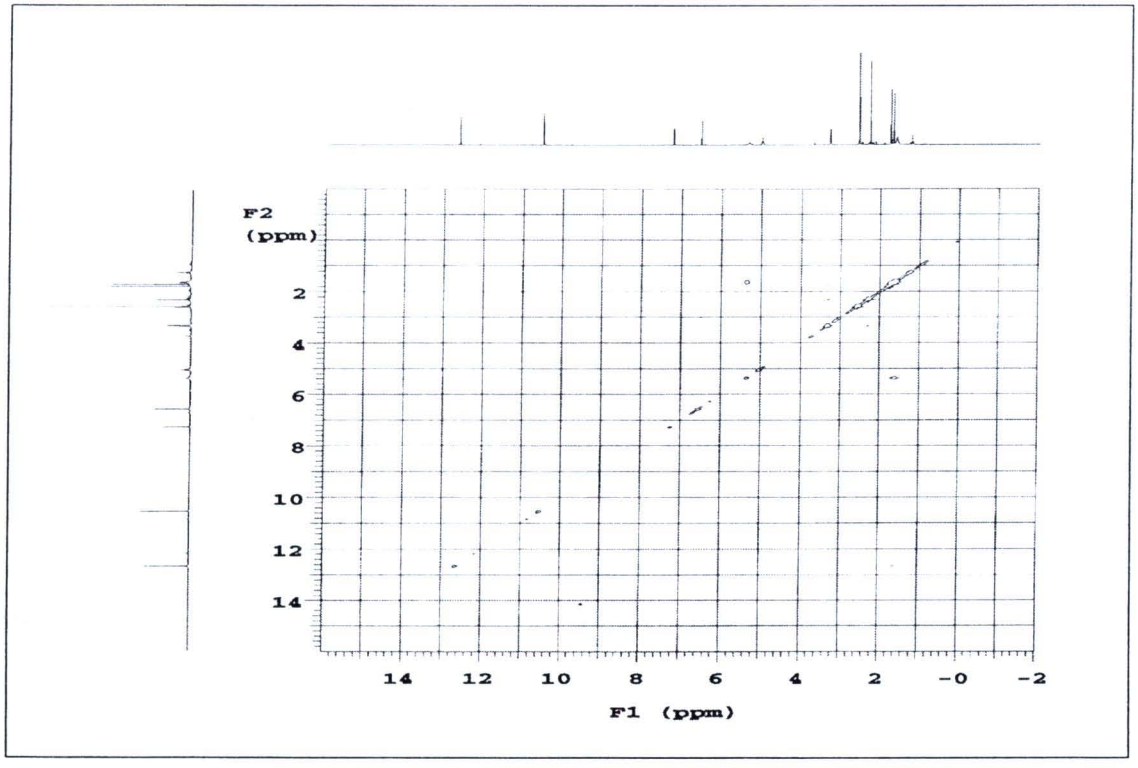

Figure 13 NOESY spectrum of mollicellin H **(1.3)**.

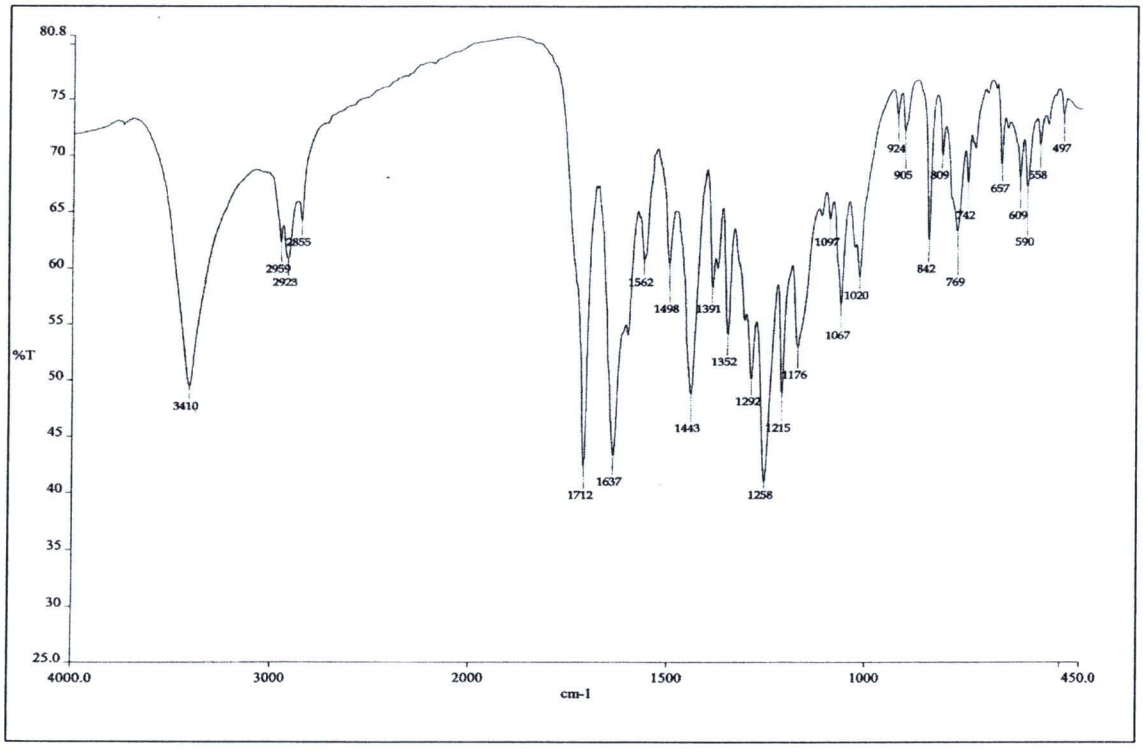

Figure 14 IR spectrum of mollicellin J **(1.4)**.

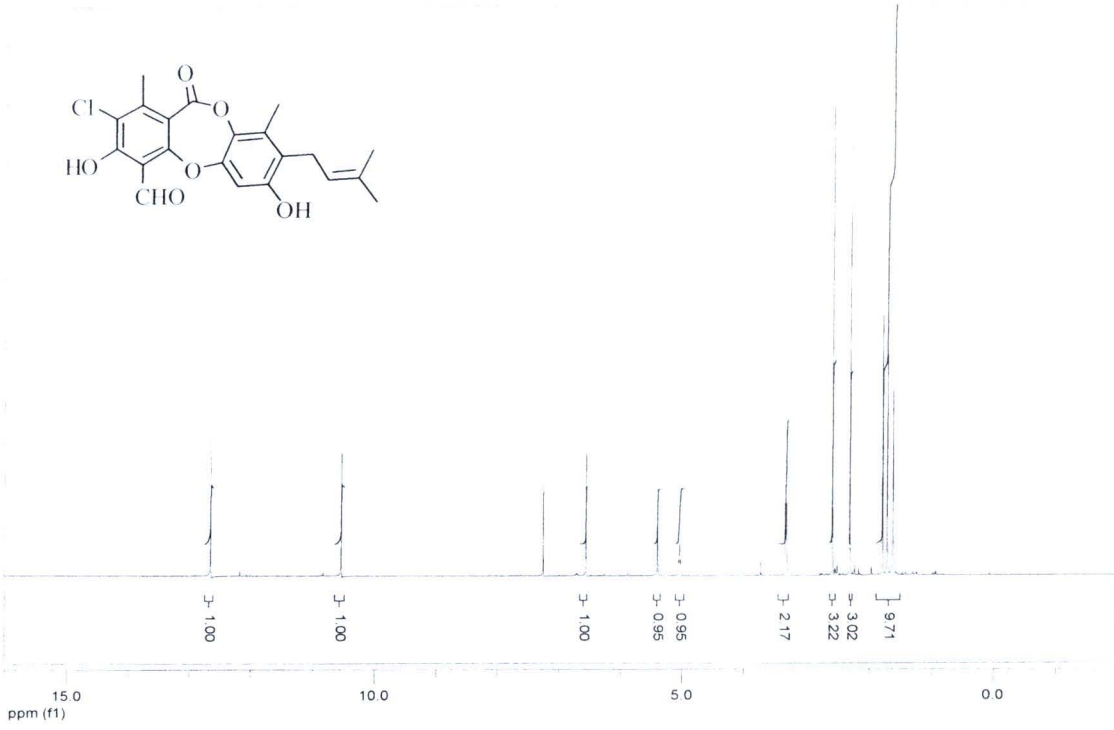

Figure 15 ^{1}H-NMR spectrum of mollicellin J **(1.4)**.

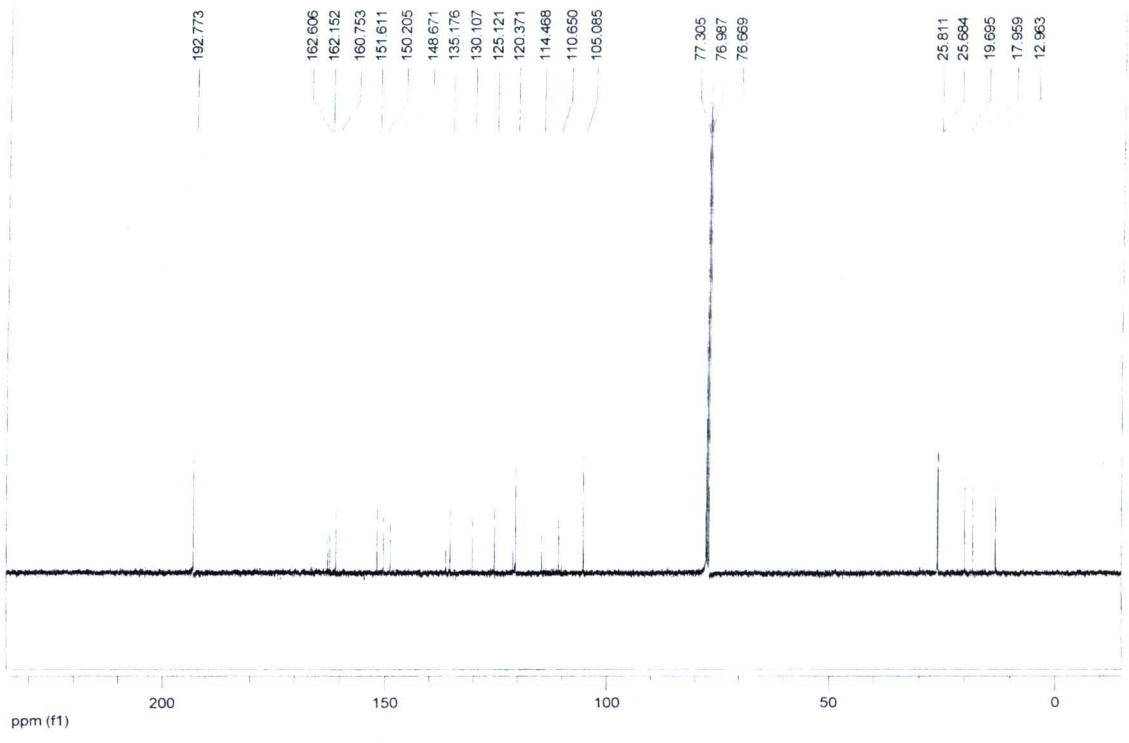

Figure 16 ^{13}C-NMR spectrum of mollicellin J **(1.4)**.

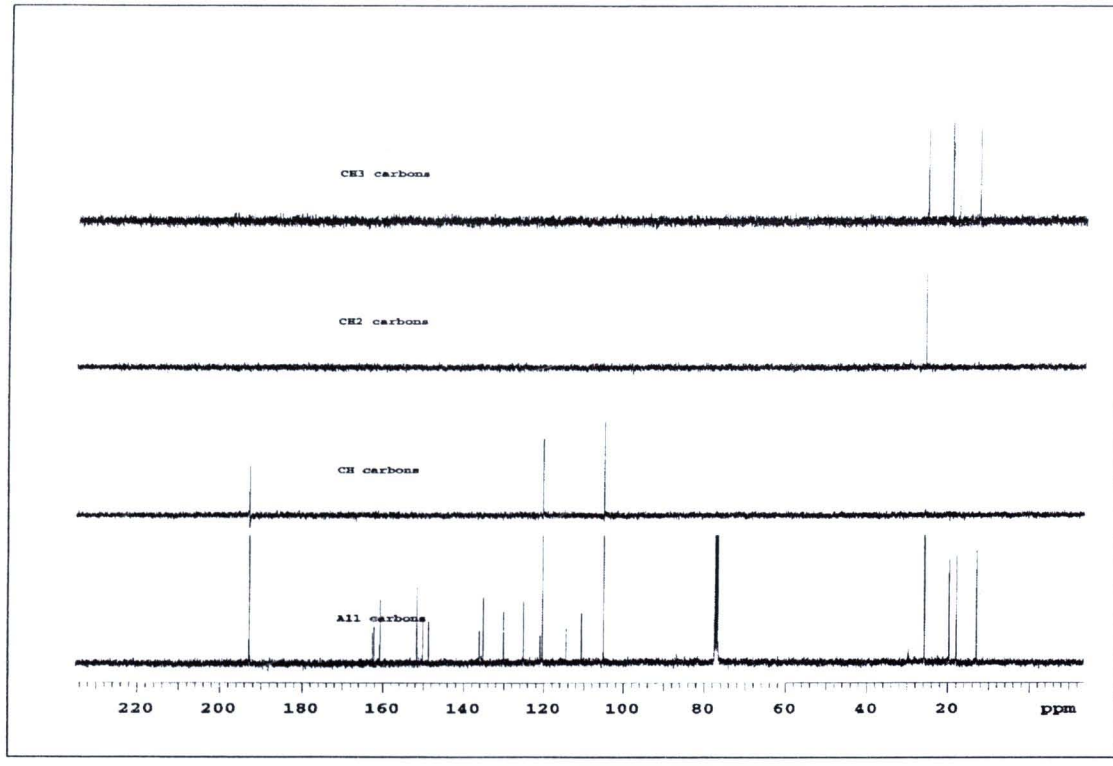

Figure 17 DEPT spectrum of mollicellin J **(1.4)**.

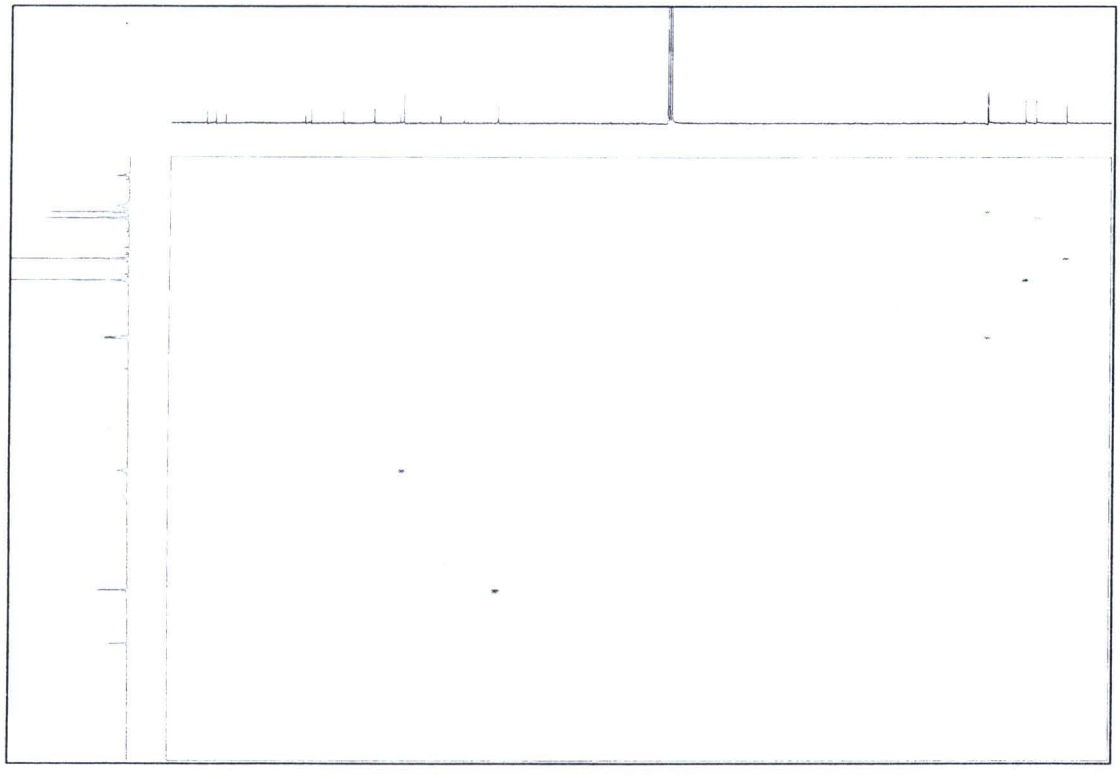

Figure 18 HSQC spectrum of mollicellin J **(1.4)**.

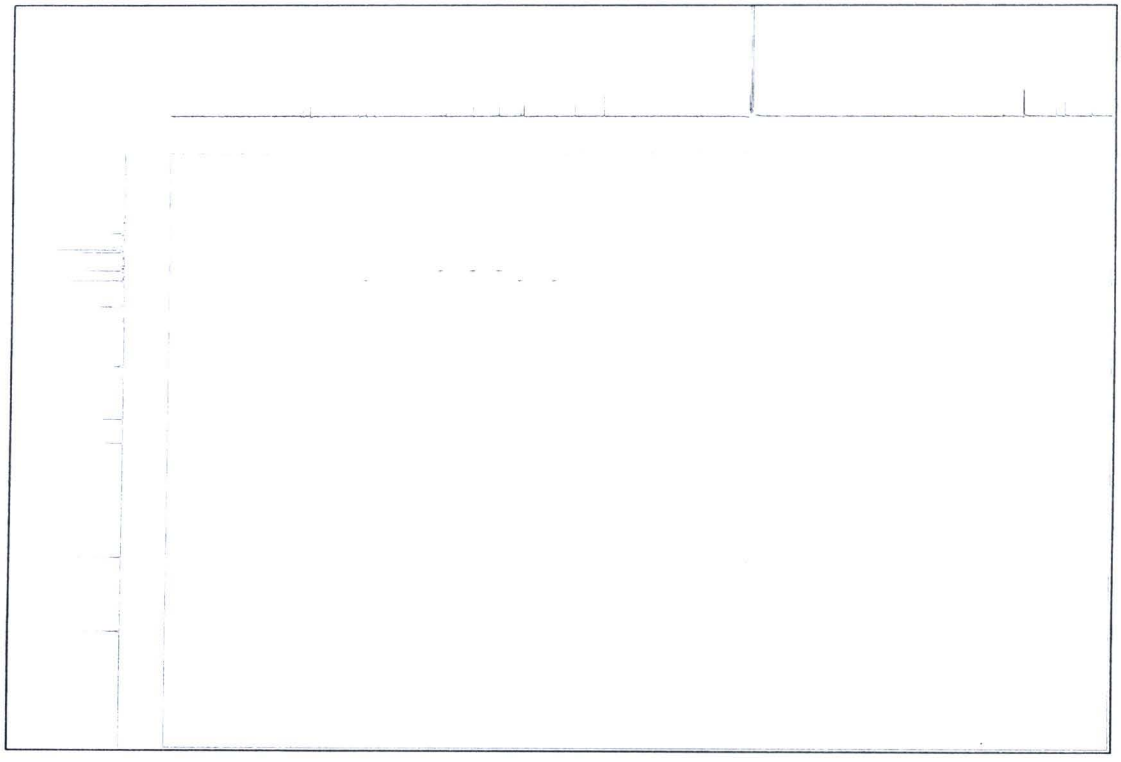

Figure 19 HMBC spectrum of mollicellin J **(1.4)**.

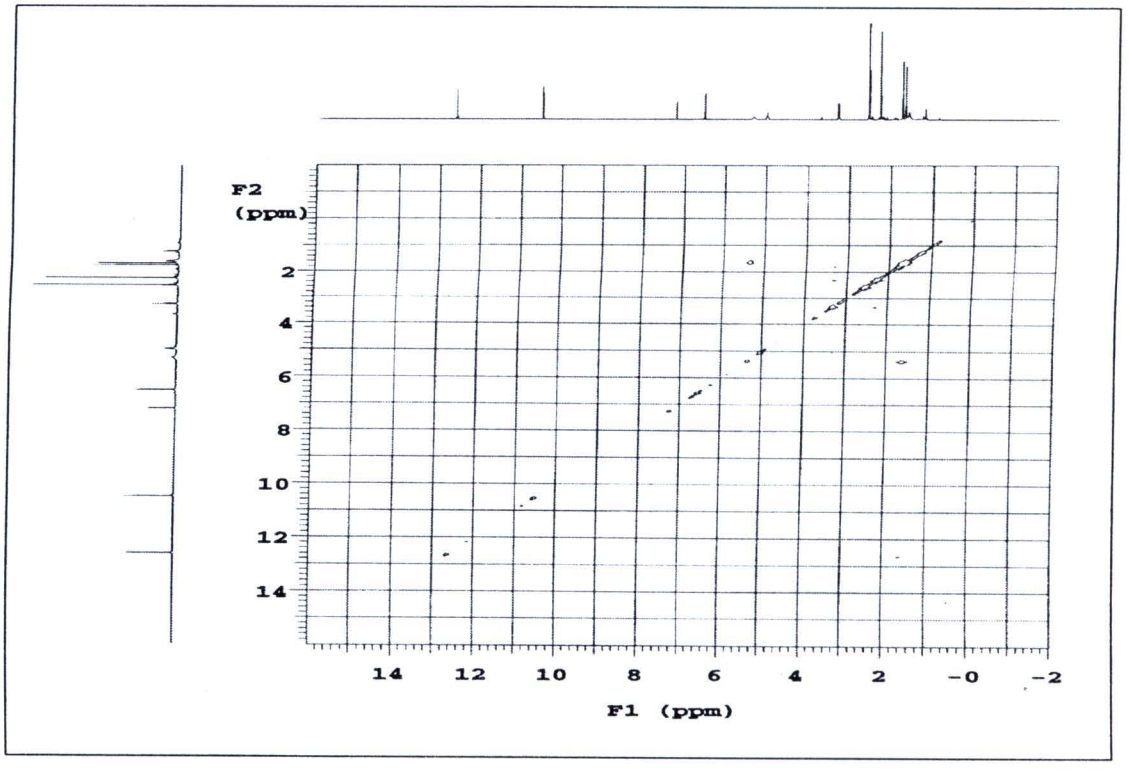

Figure 20 NOESY spectrum of mollicellin J **(1.4)**.

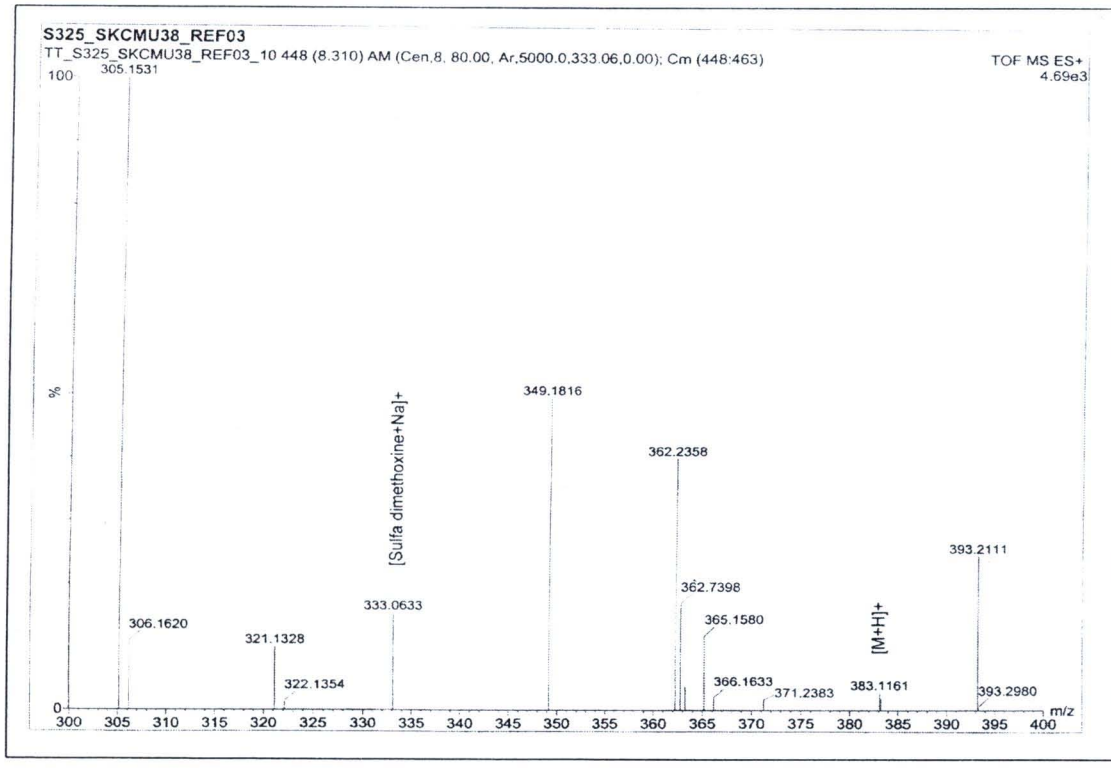

Figure 21 Mass spectrum of mollicellin K **(1.5)**.

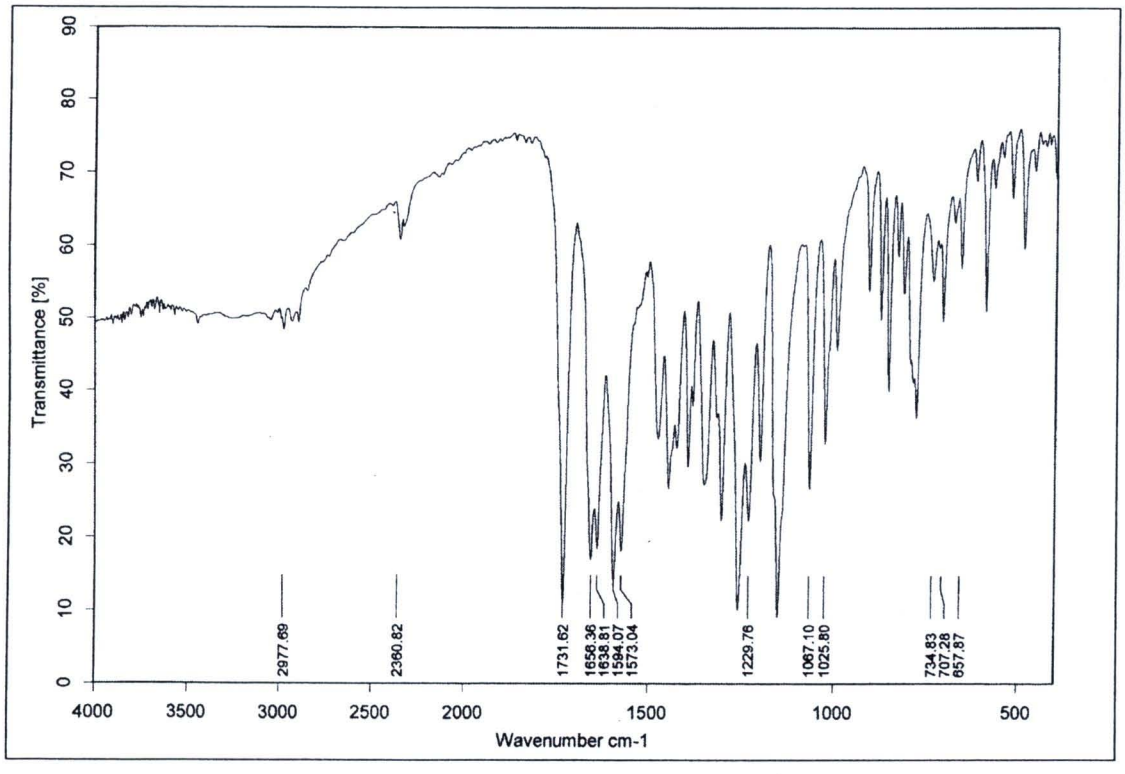

Figure 22 IR spectrum of mollicellin K **(1.5)**.

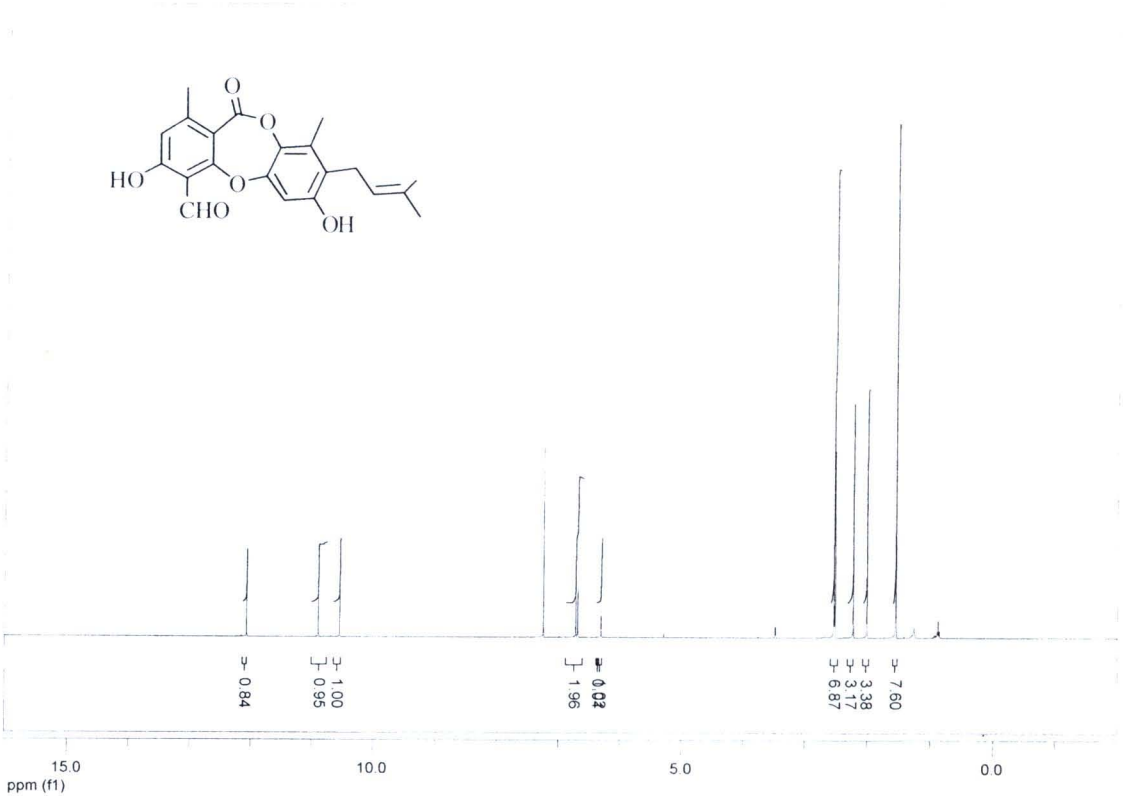

Figure 23 ^{1}H-NMR spectrum of mollicellin K **(1.5)**.

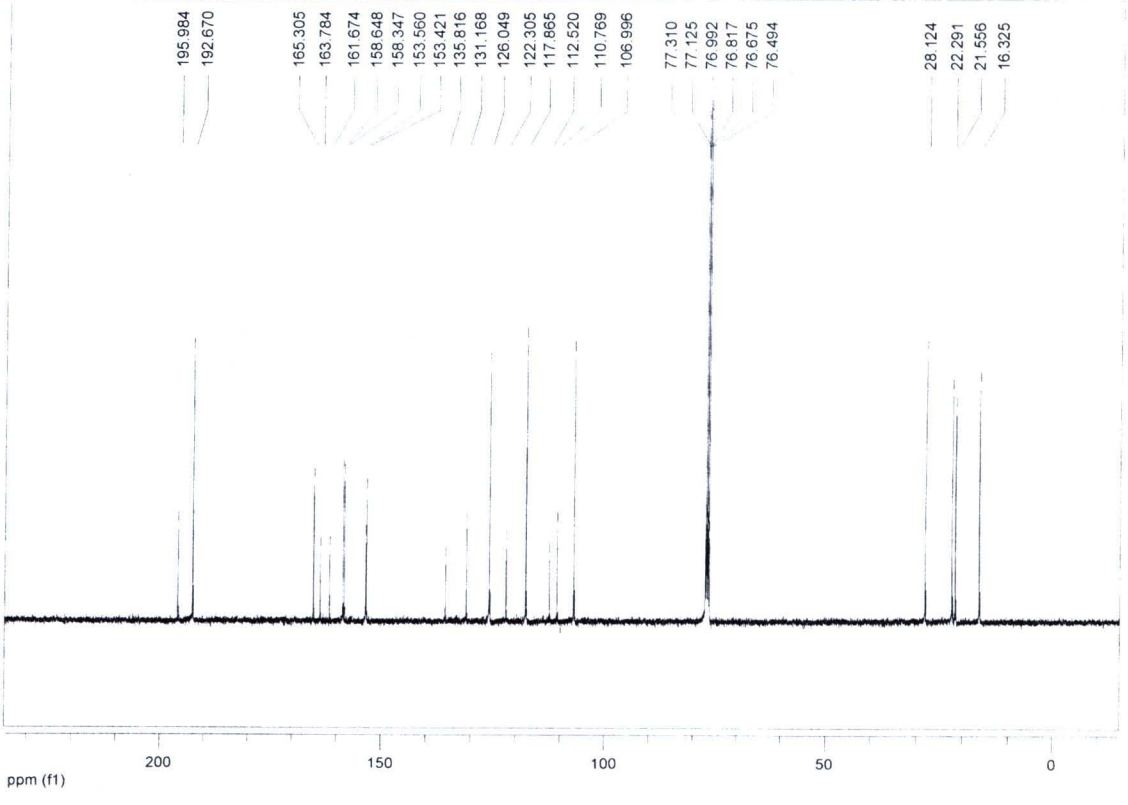

Figure 24 ^{13}C-NMR spectrum of mollicellin K **(1.5)**.

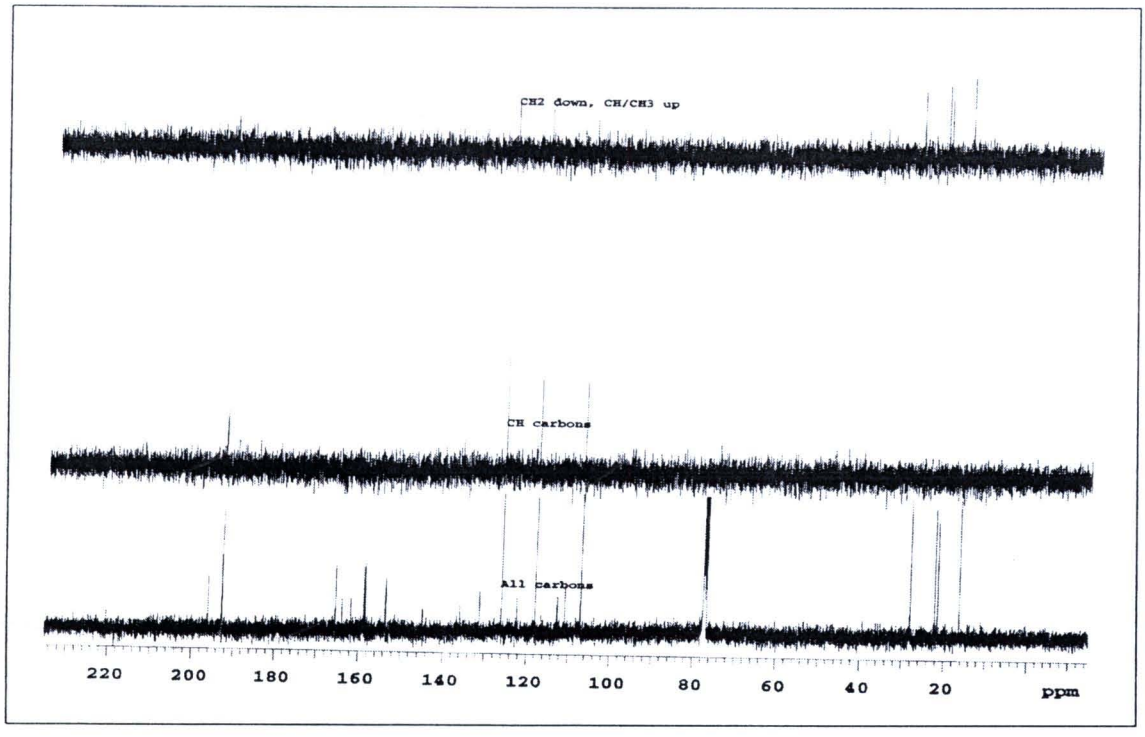

Figure 25 DEPT spectrum of mollicellin K **(1.5)**.

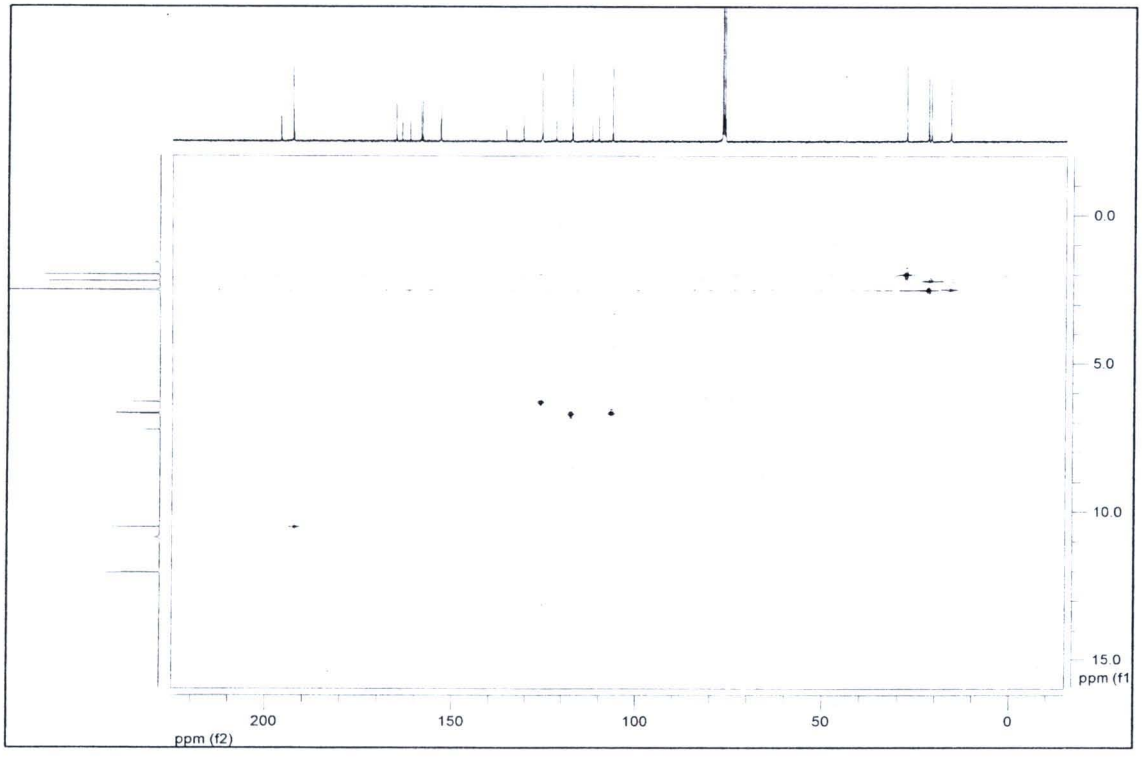

Figure 26 HSQC spectrum of mollicellin K **(1.5)**.

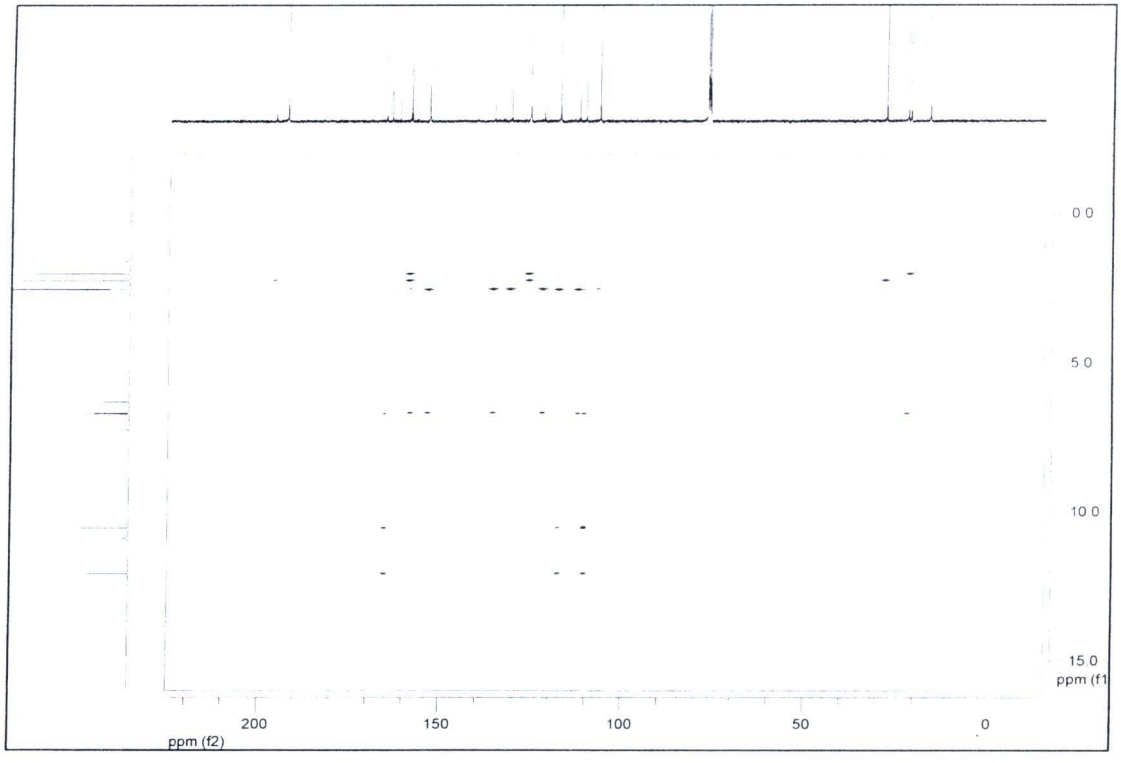

Figure 27 HMBC spectrum of mollicellin K **(1.5)**.

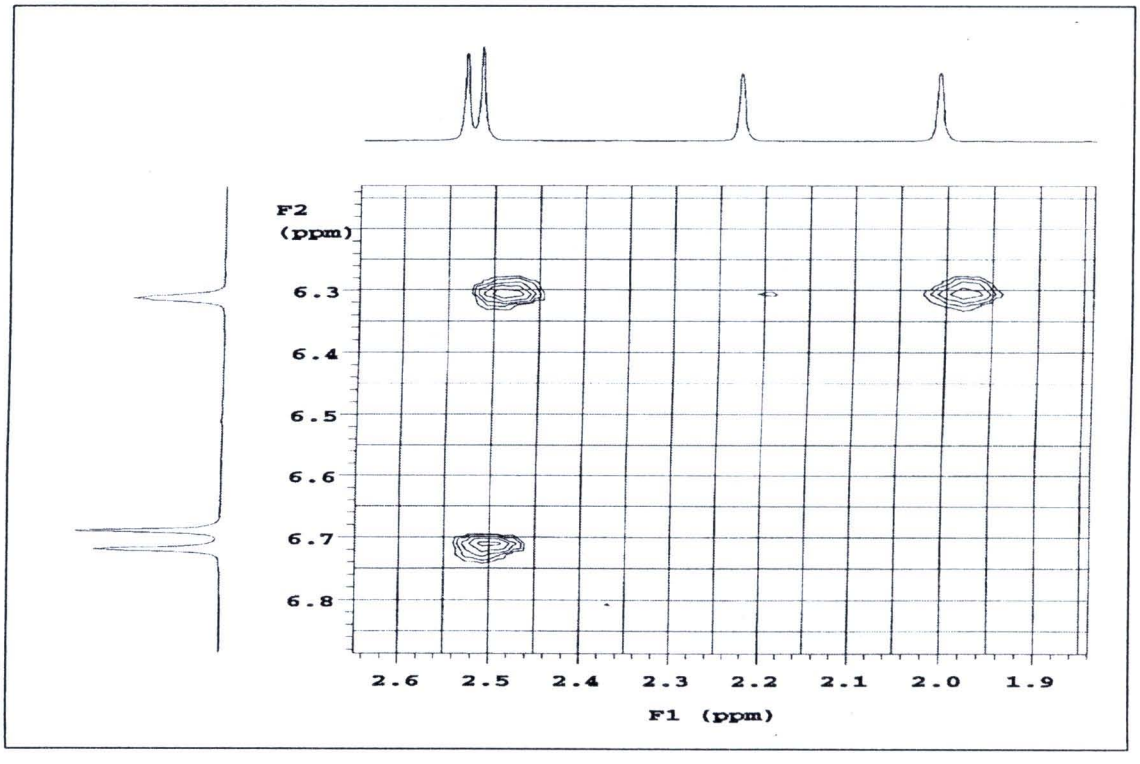

Figure 28 NOESY spectrum of mollicellin K **(1.5).**

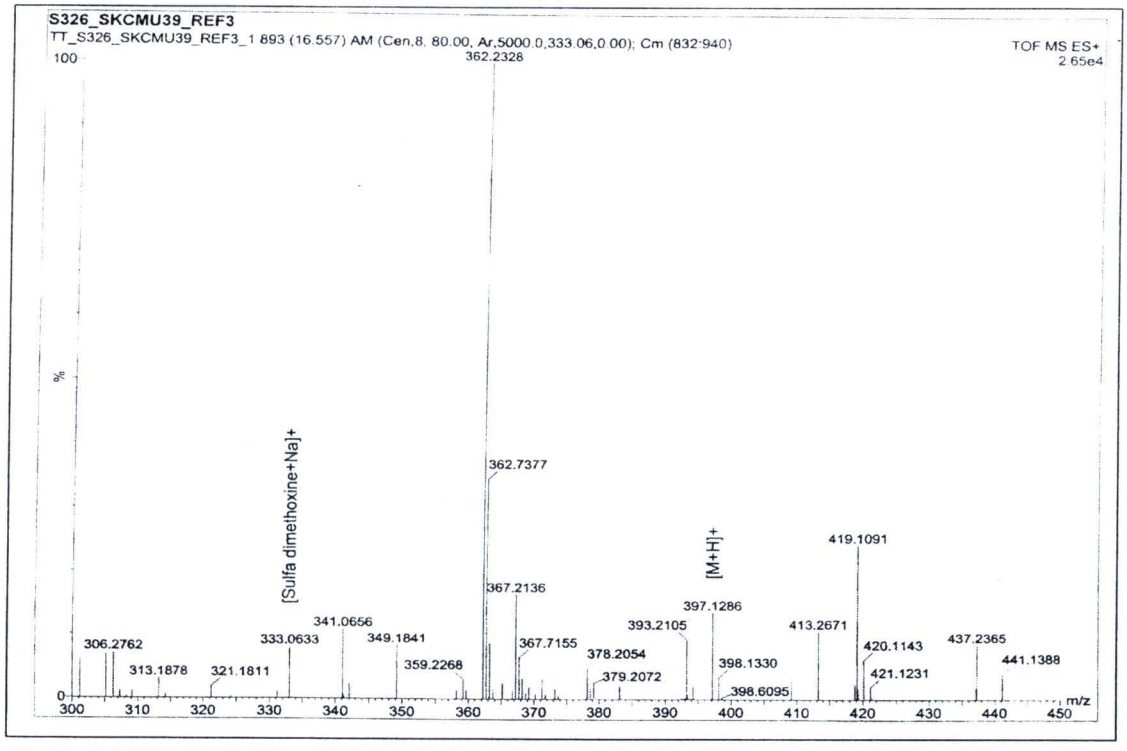

Figure 29 Mass spectrum of mollicellin L **(1.6)**.

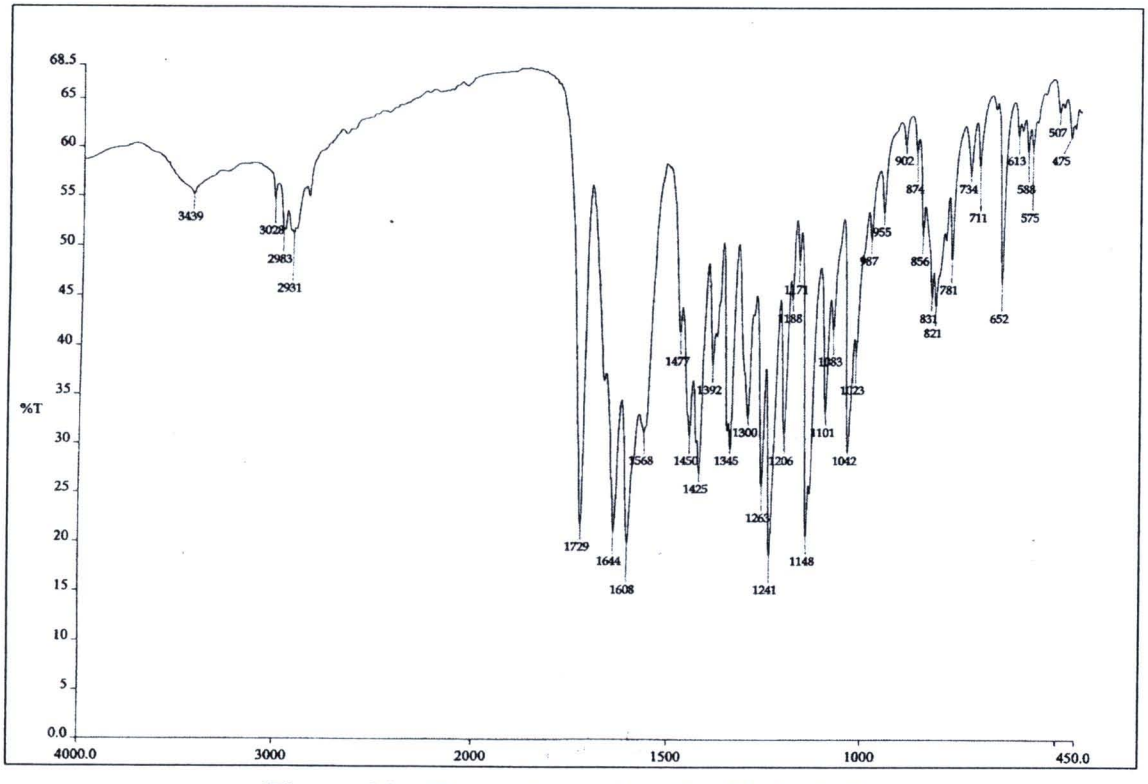

Figure 30 IR spectrum of mollicellin L **(1.6)**.

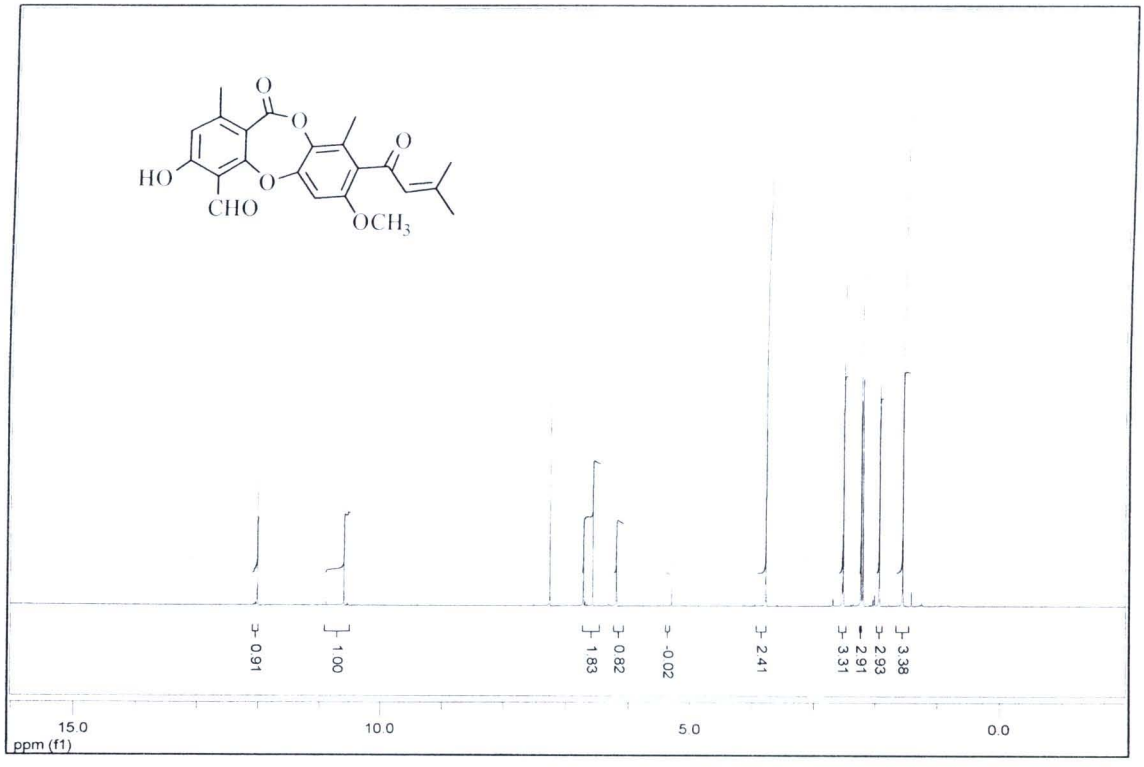

Figure 31 ^{1}H-NMR spectrum of mollicellin L **(1.6).**

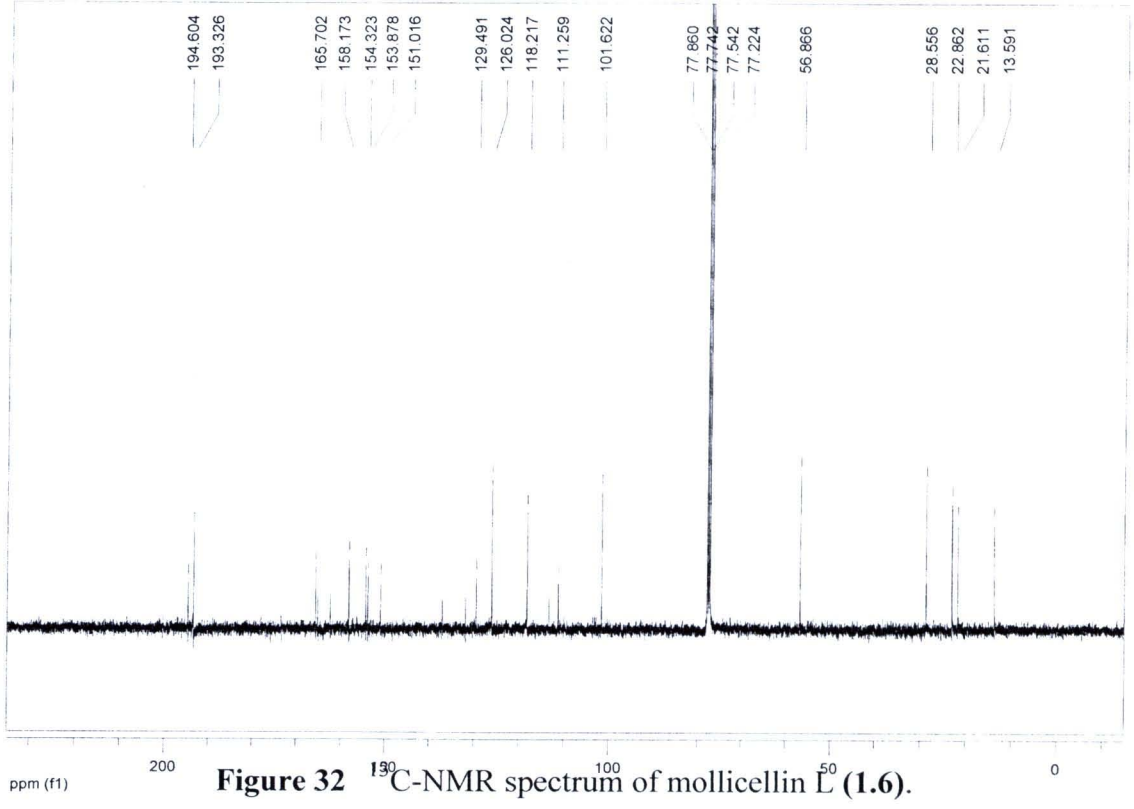

Figure 32 ^{13}C-NMR spectrum of mollicellin L **(1.6).**

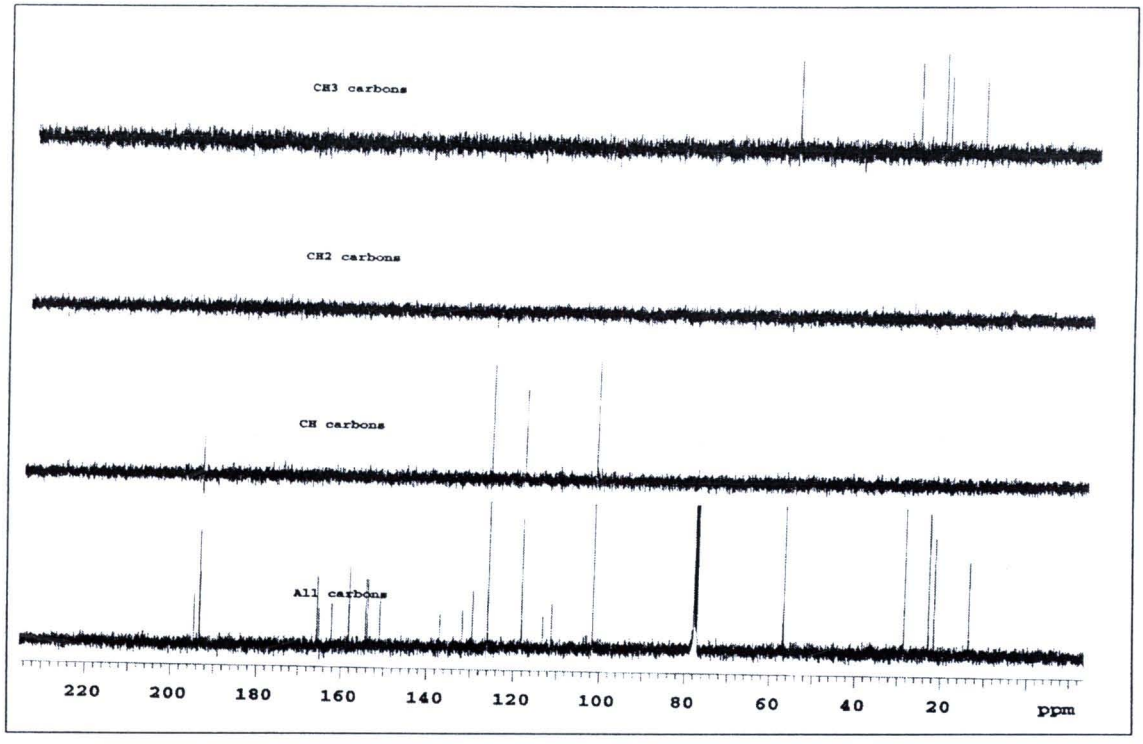

Figure 33 DEPT spectrum of mollicellin L **(1.6)**.

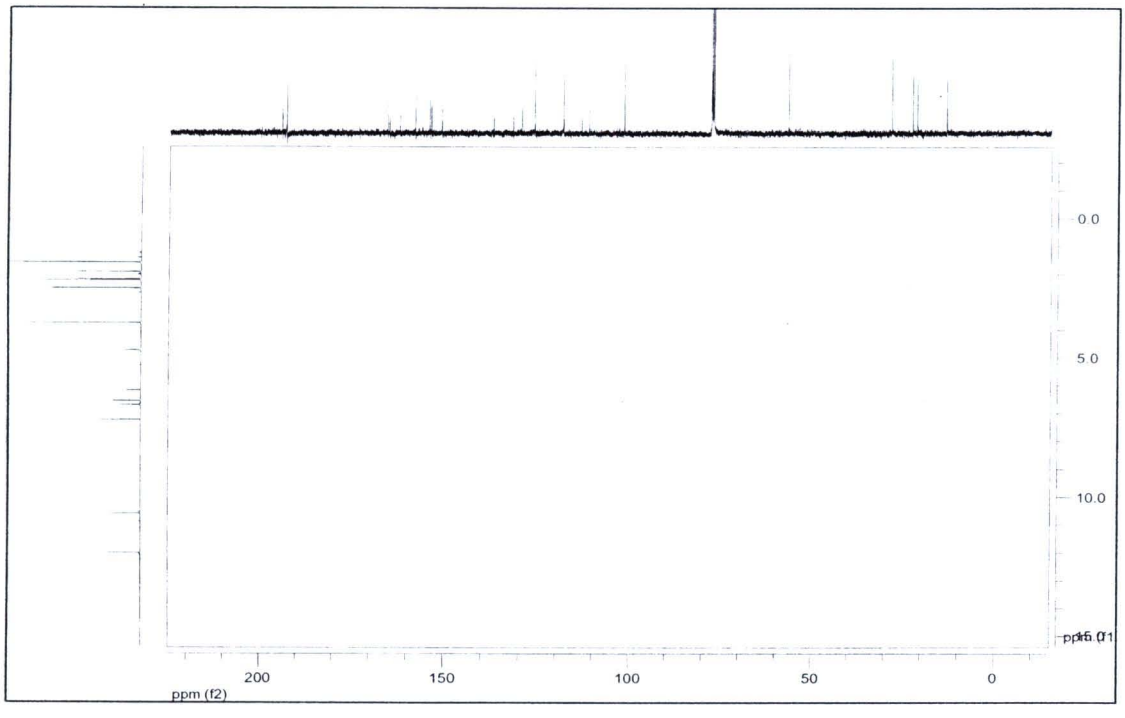

Figure 34 HSQC spectrum of mollicellin L **(1.6)**.

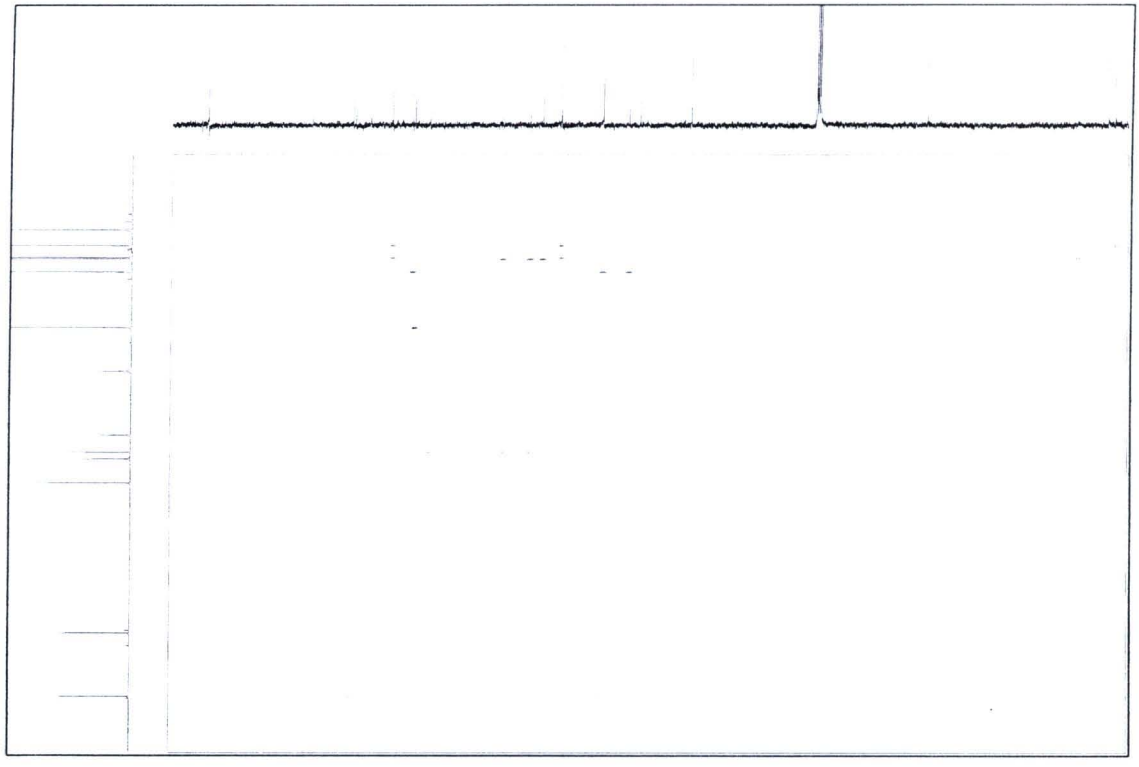

Figure 35 HMBC spectrum of mollicellin L **(1.6)**.

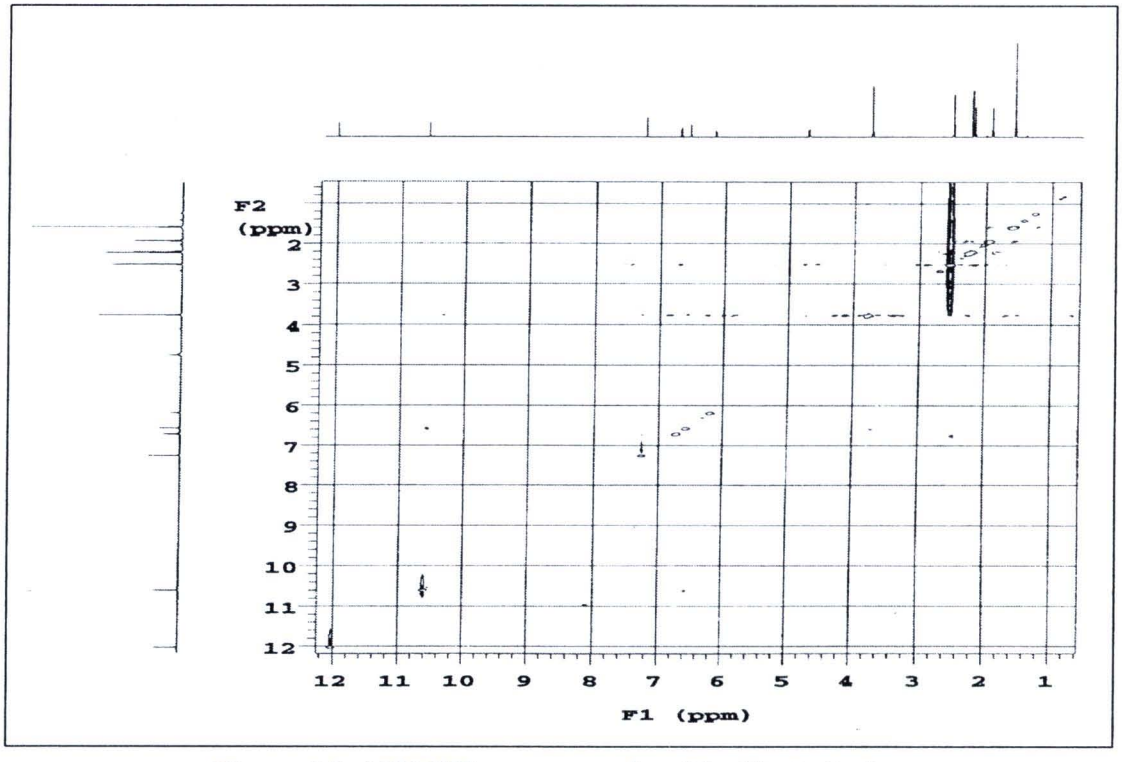

Figure 36 NOESY spectrum of mollicellin L **(1.6)**.

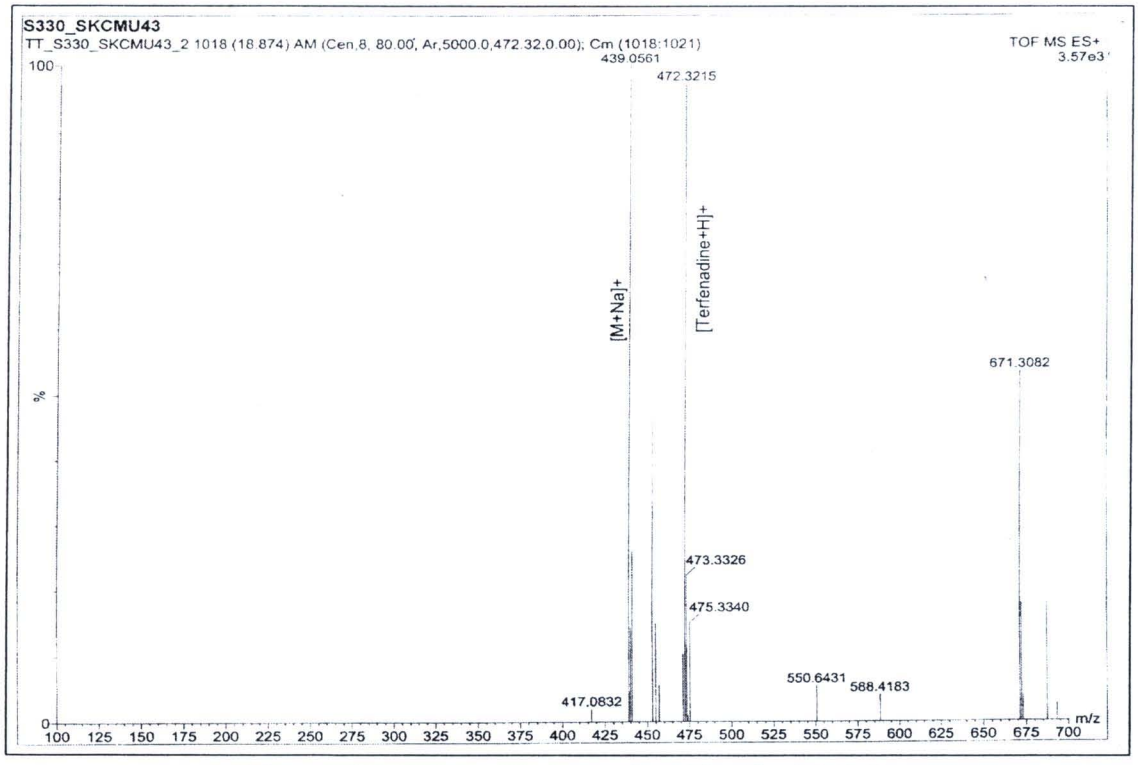

Figure 37 Mass spectrum of mollicellin M **(1.7)**.

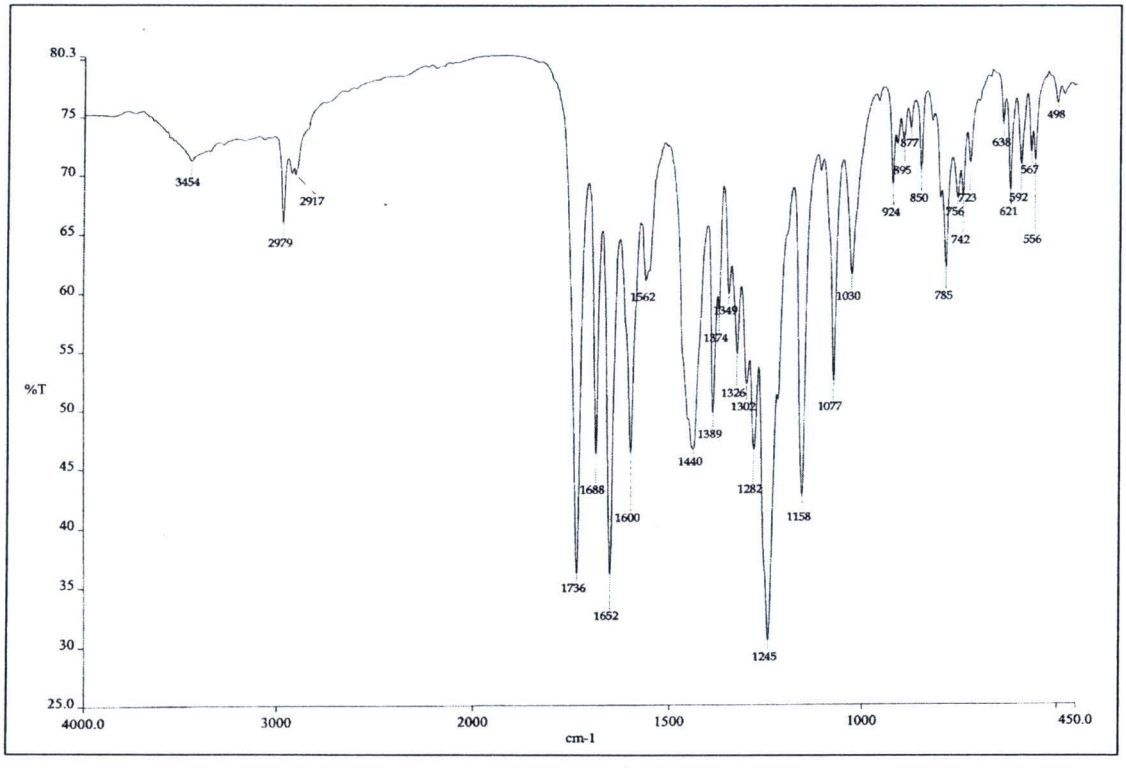

Figure 38 IR spectrum of mollicellin M **(1.7).**

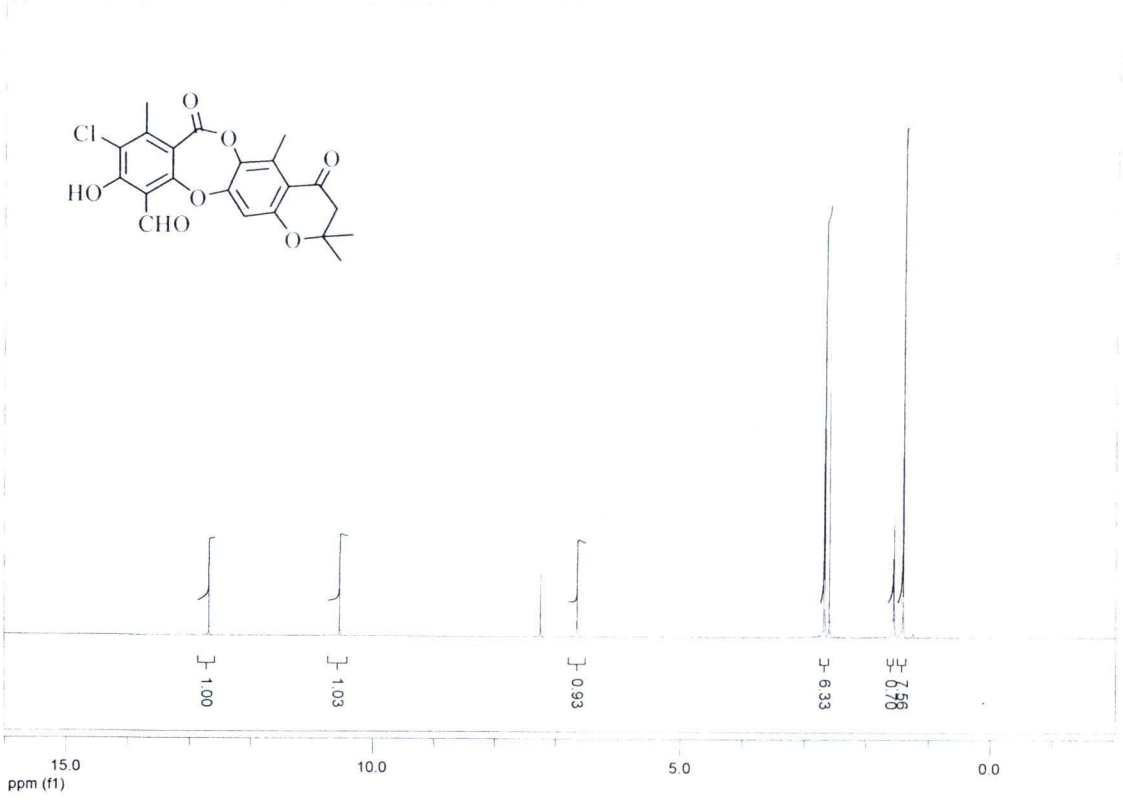

Figure 39 ^{1}H-NMR spectrum of mollicellin M **(1.7)**.

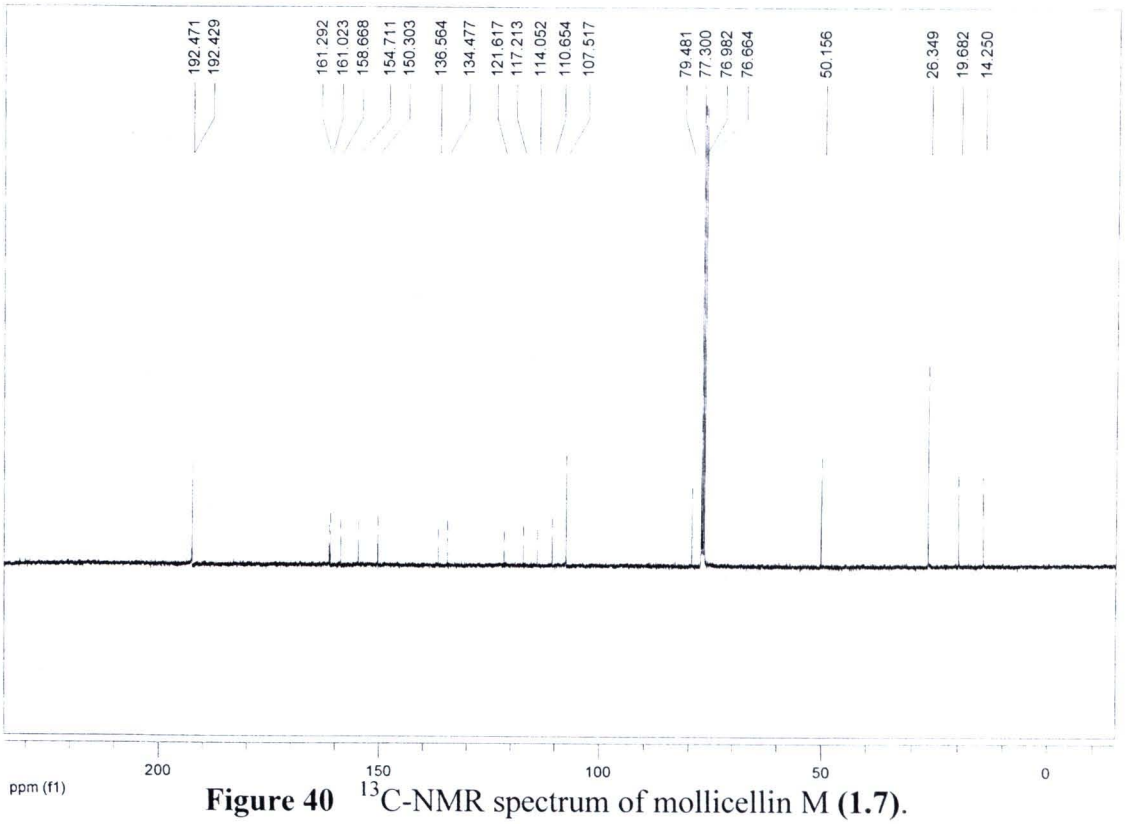

Figure 40 ^{13}C-NMR spectrum of mollicellin M **(1.7)**.

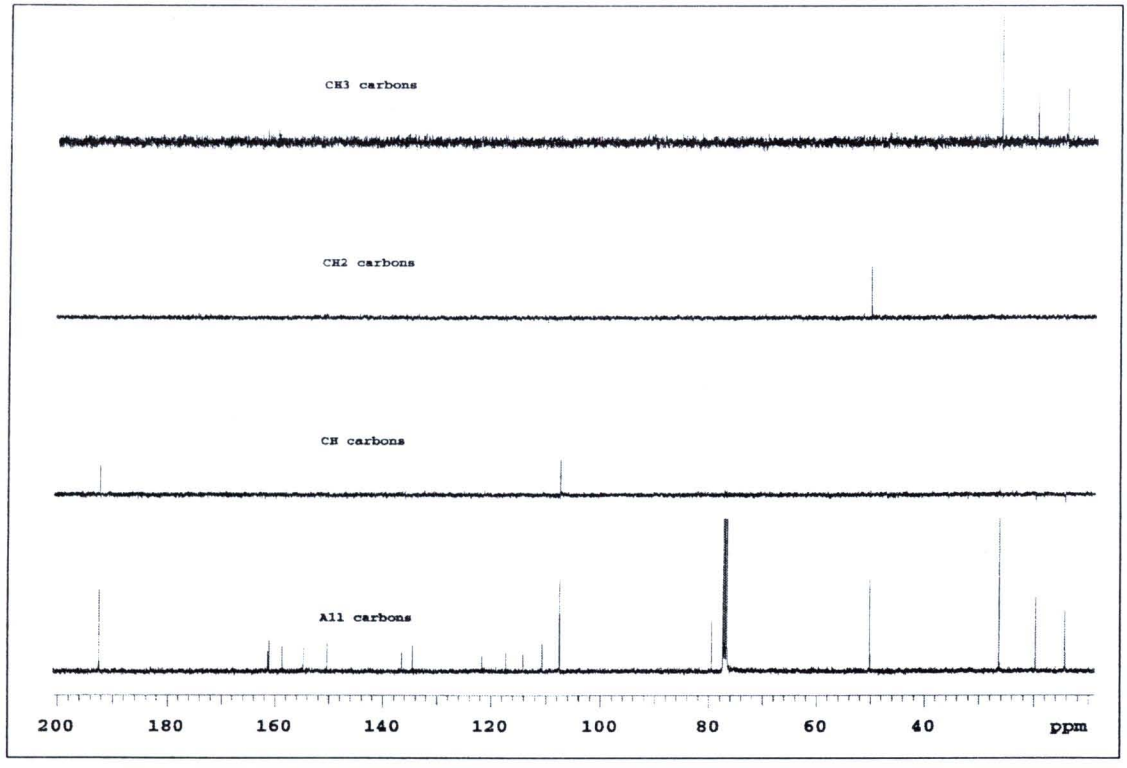

Figure 41 DEPT spectrum of mollicellin M **(1.7)**.

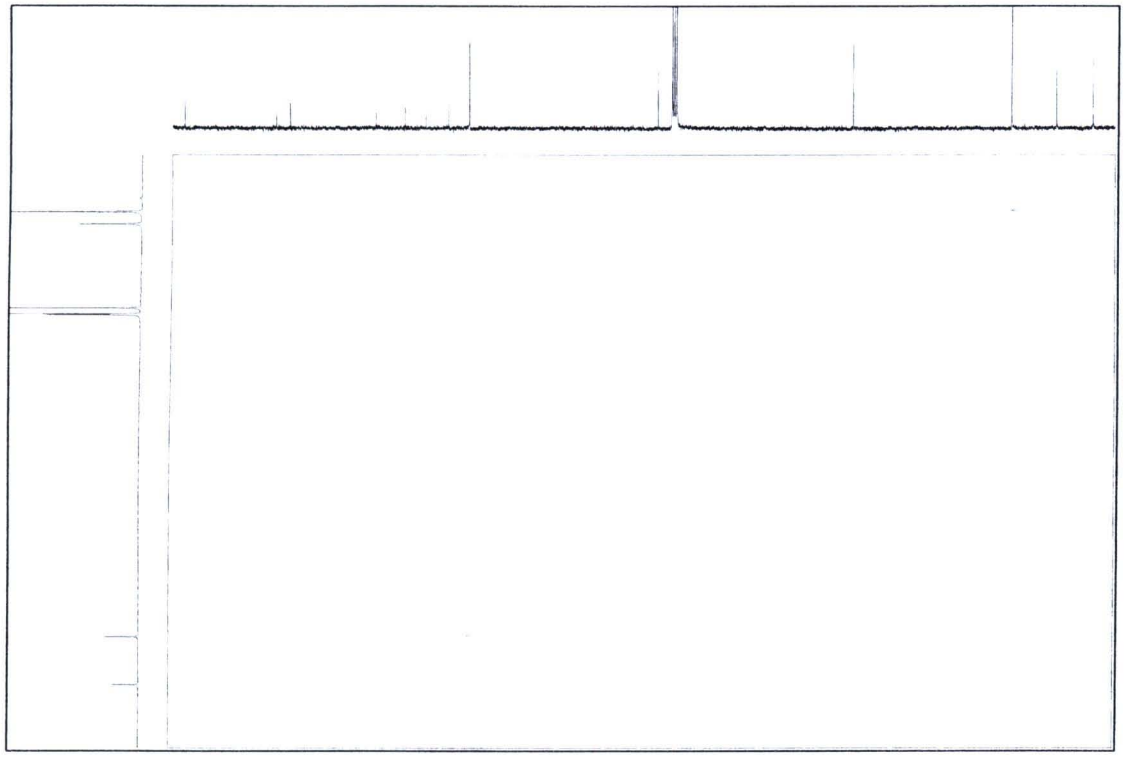

Figure 42 HSQC spectrum of mollicellin M **(1.7).**

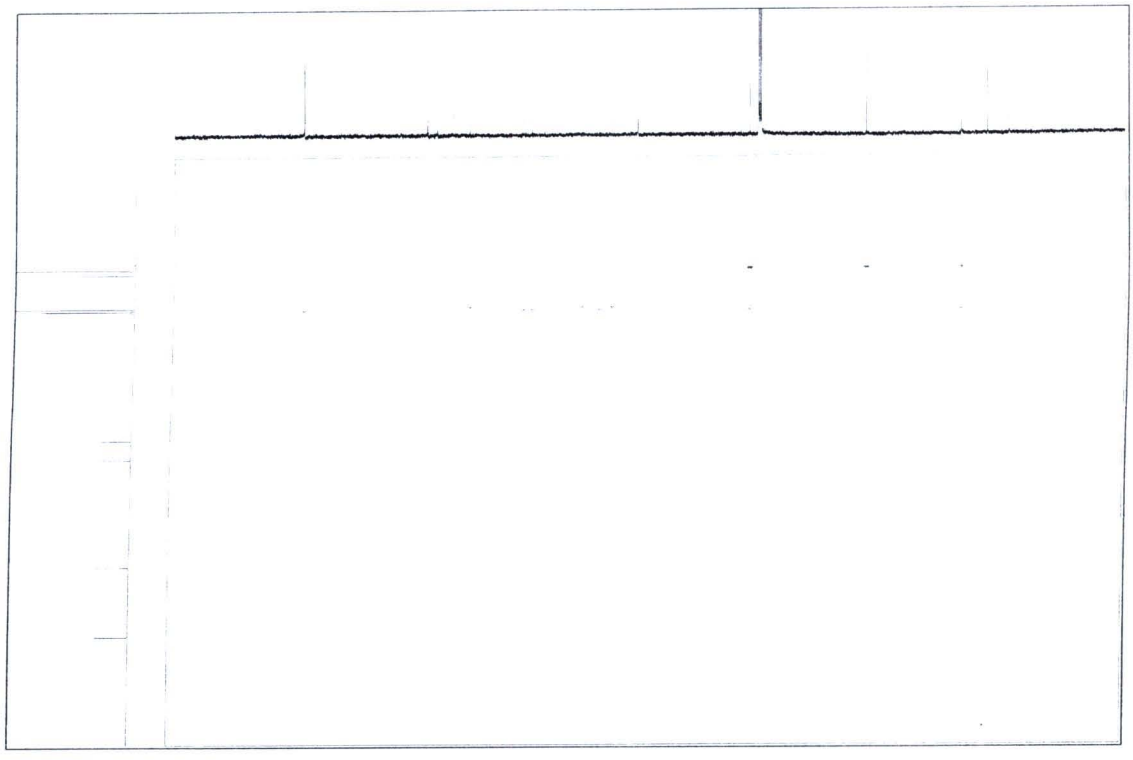

Figure 43 HMBC spectrum of mollicellin M **(1.7)**.

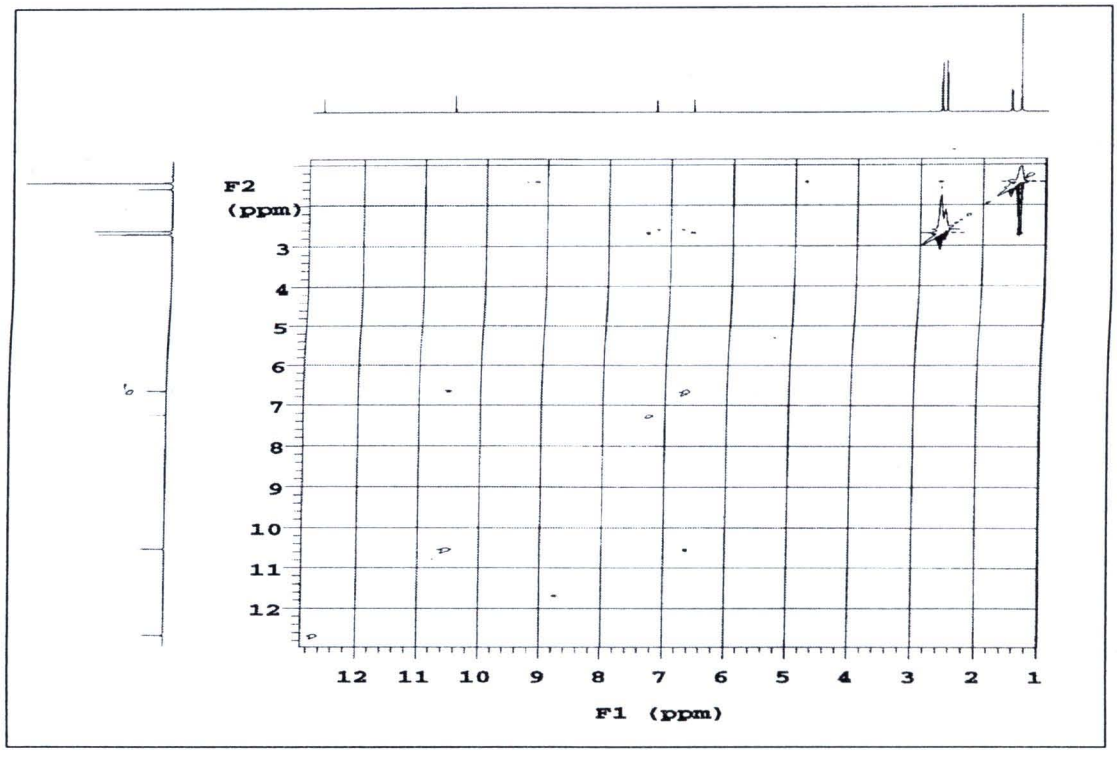

Figure 44 NOESY spectrum of mollicellin M **(1.7).**

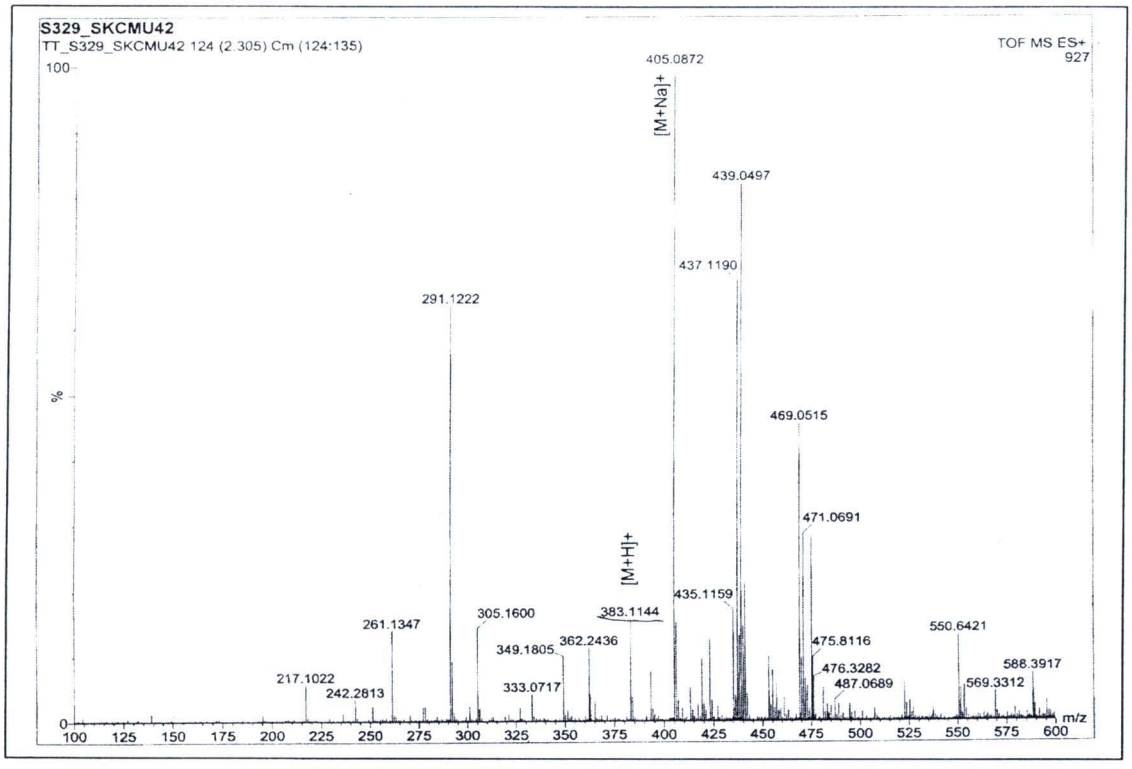

Figure 45 Mass spectrum of mollicellin B **(1.8)**.

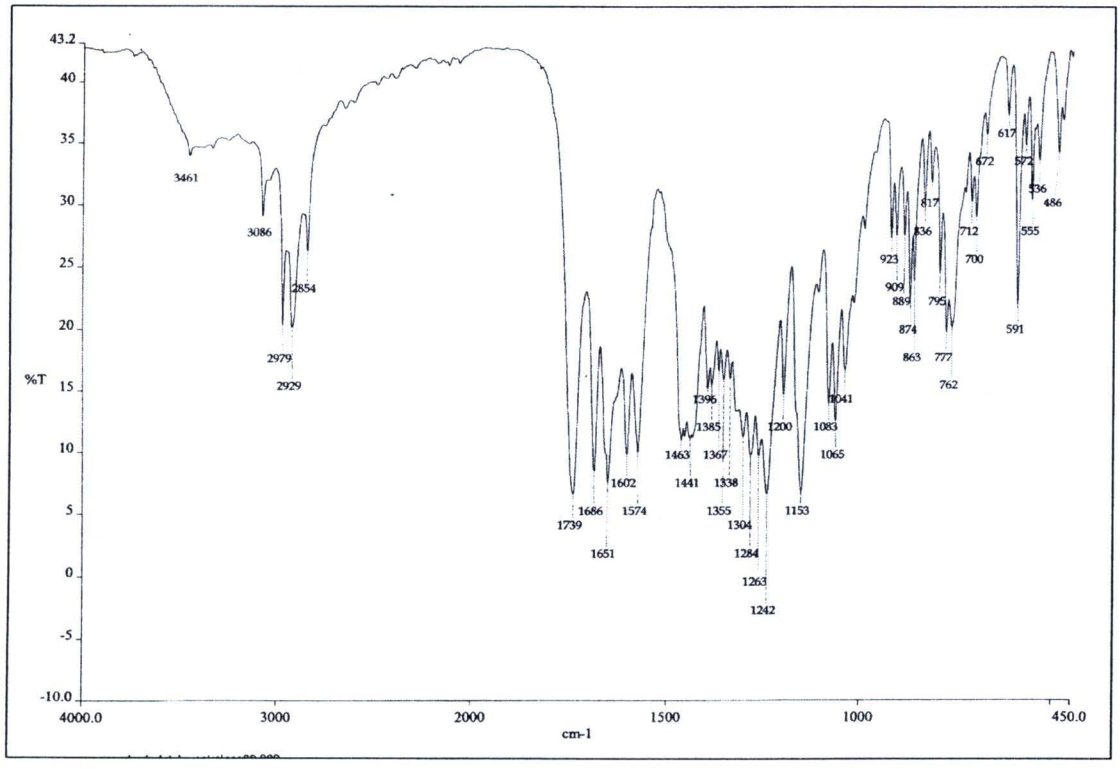

Figure 46 IR spectrum of mollicellin B **(1.8)**.

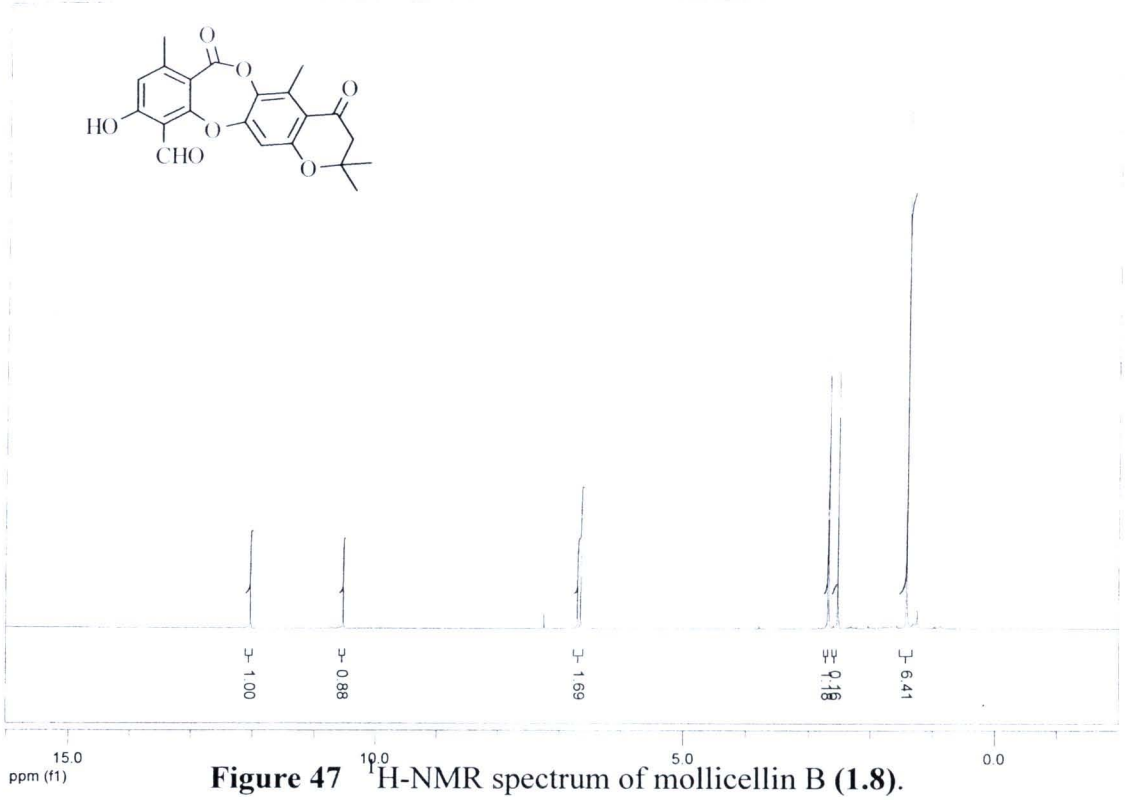

Figure 47 ^{1}H-NMR spectrum of mollicellin B **(1.8)**.

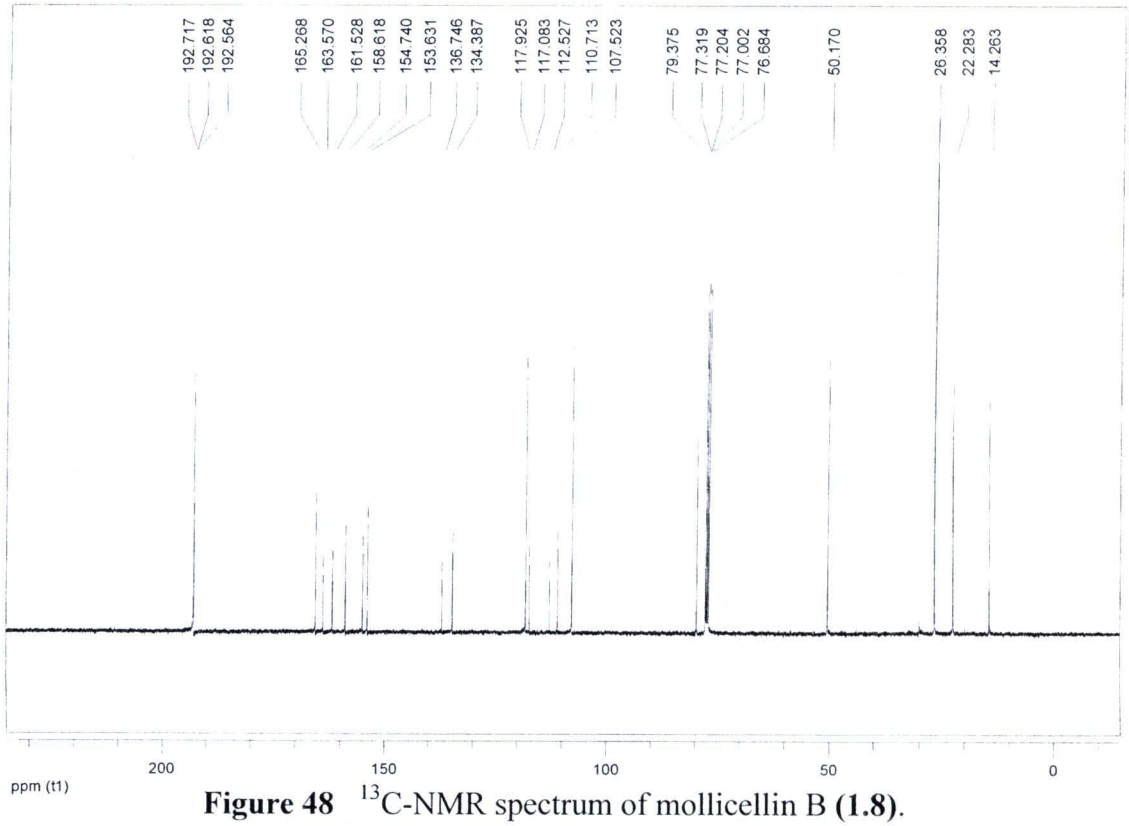

Figure 48 ^{13}C-NMR spectrum of mollicellin B **(1.8)**.

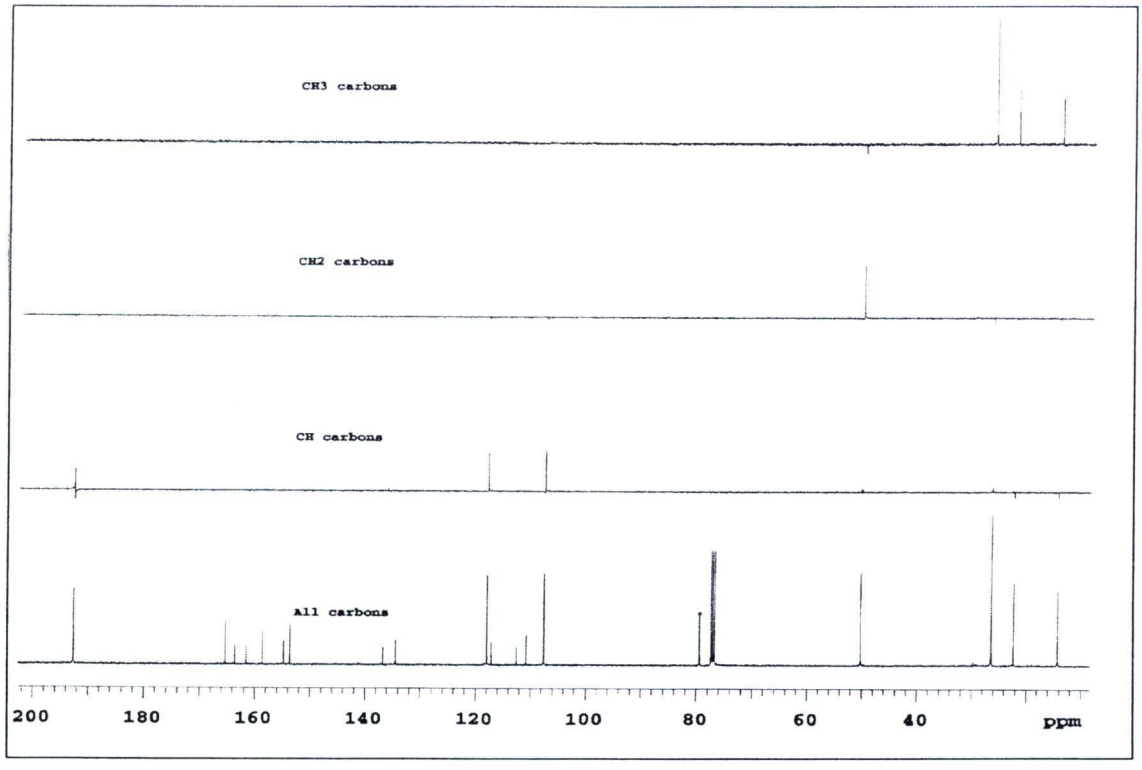

Figure 49 DEPT spectrum of mollicellin B **(1.8)**.

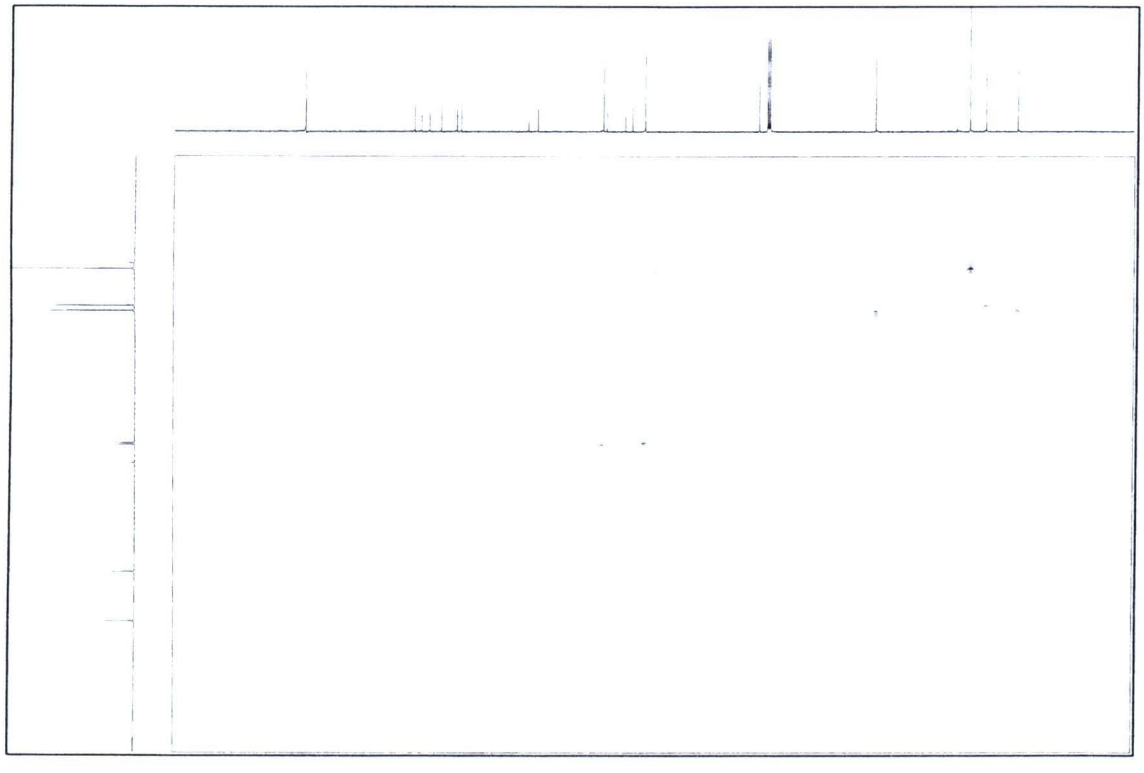

Figure 50 HSQC spectrum of mollicellin B **(1.8)**.

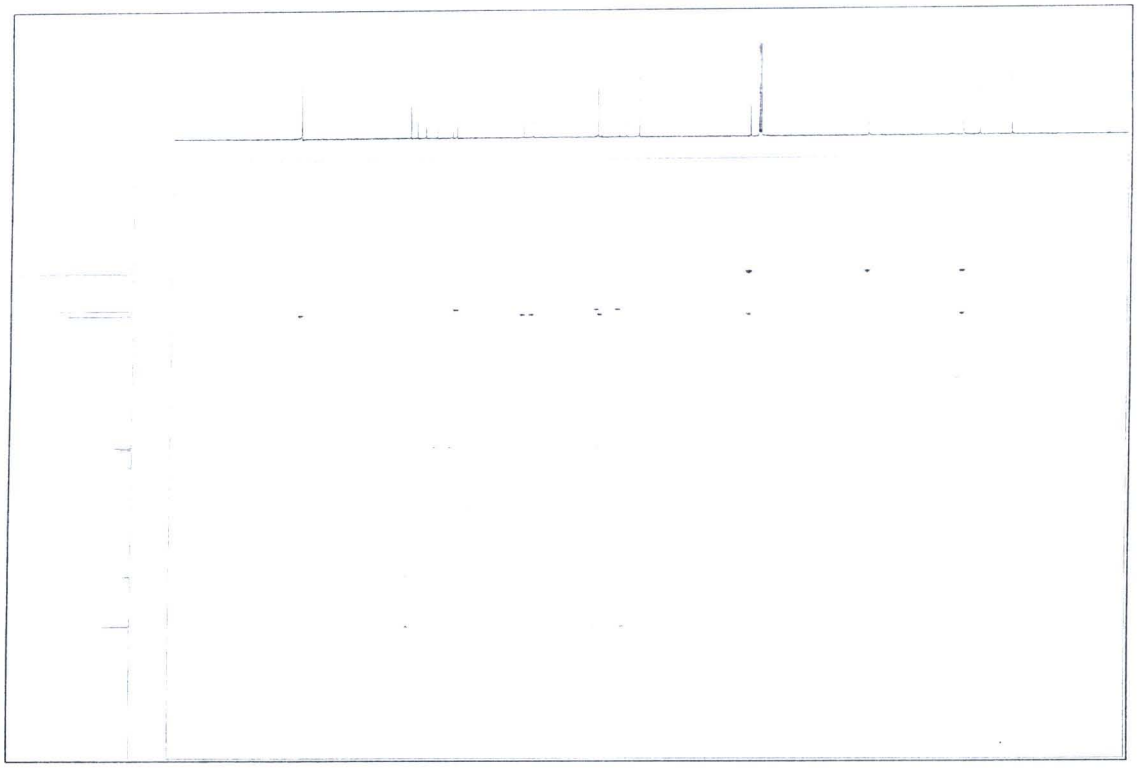

Figure 51 HMBC spectrum of mollicellin B **(1.8).**

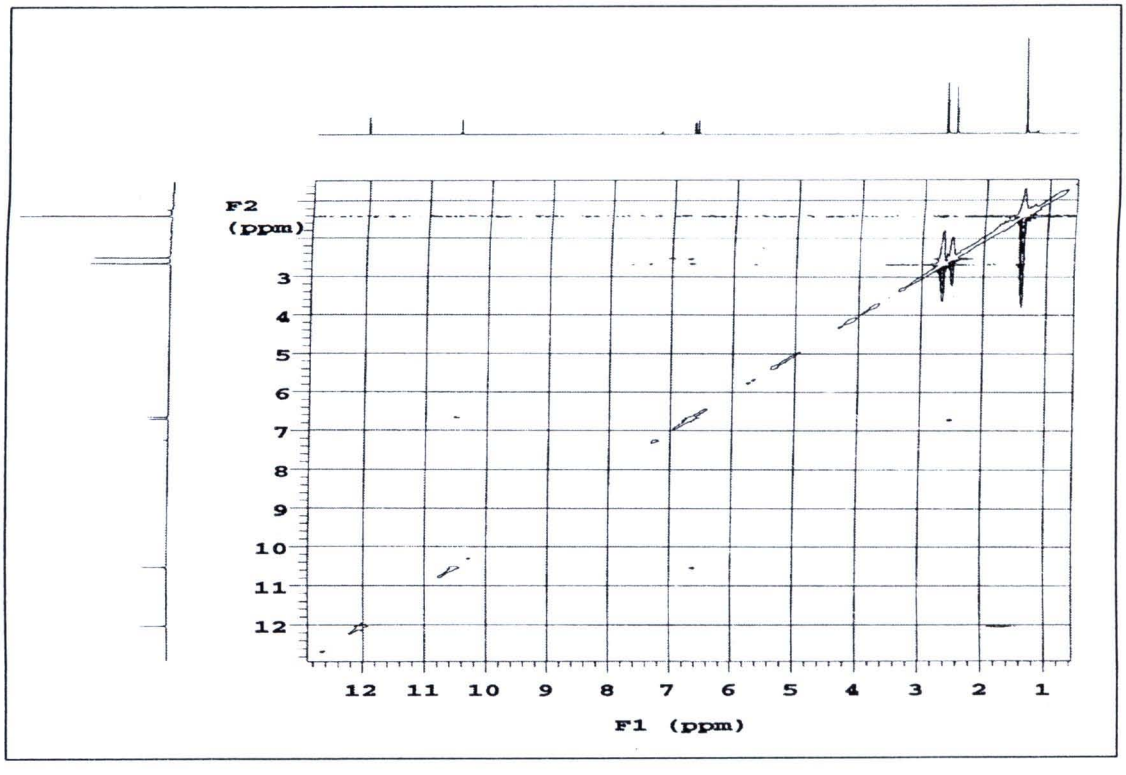

Figure 52 NOESY spectrum of mollicellin B **(1.8)**.

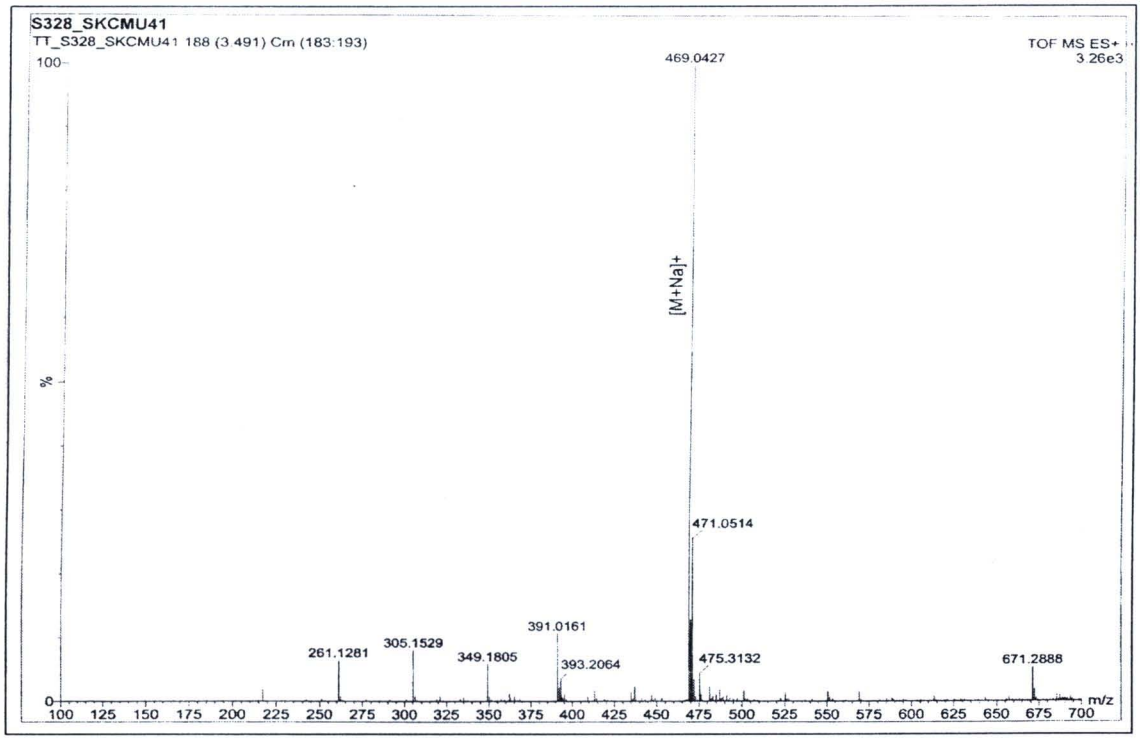

Figure 53 Mass spectrum of mollicellin C **(1.9)**.

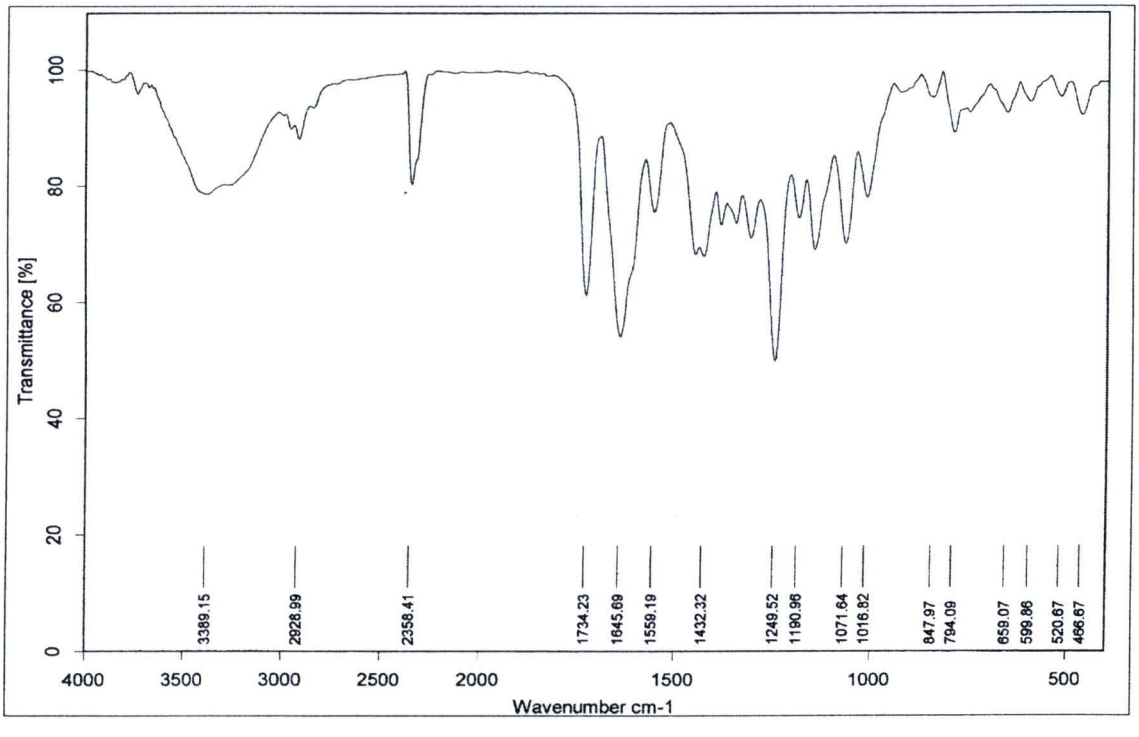

Figure 54 IR spectrum of mollicellin C **(1.9).**

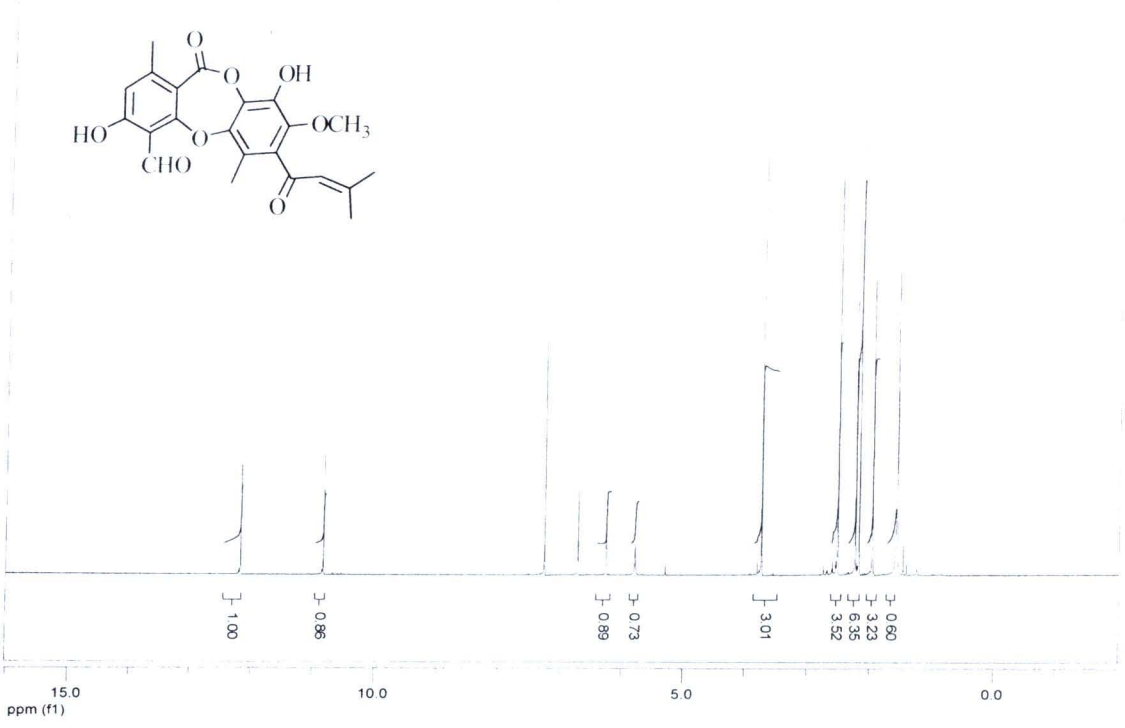

Figure 55 ^{1}H-NMR spectrum of mollicellin C **(1.9)**.

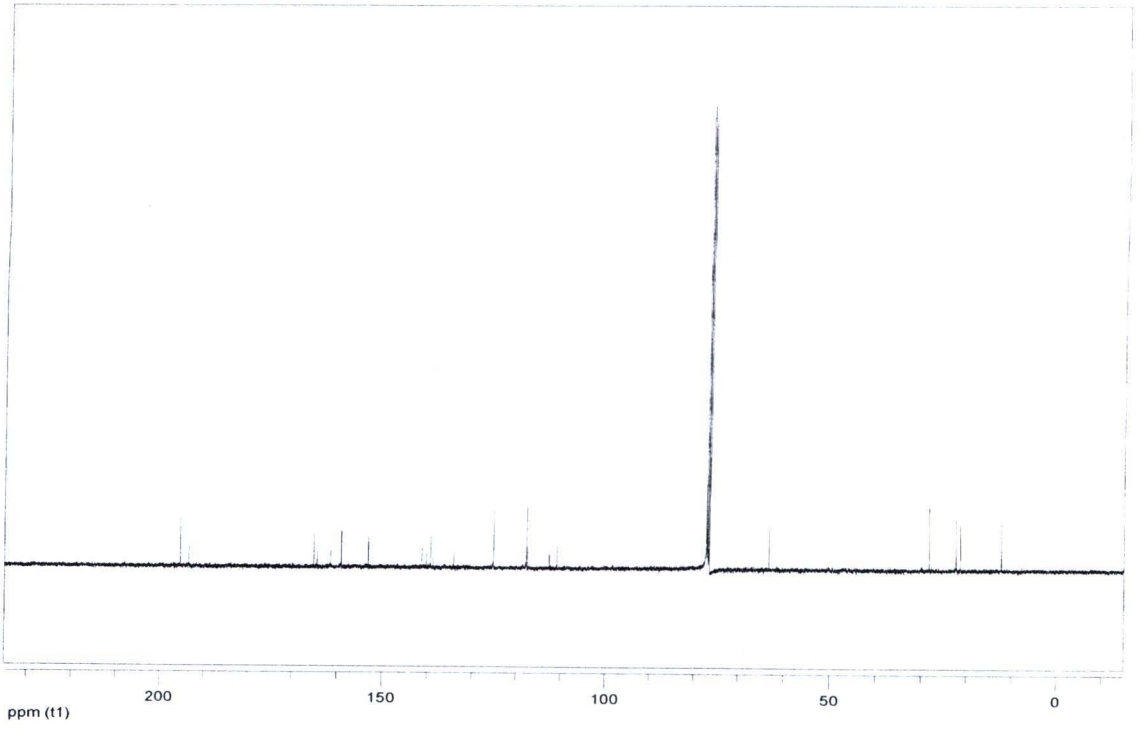

Figure 56 ^{13}C-NMR spectrum of mollicellin C **(1.9)**.

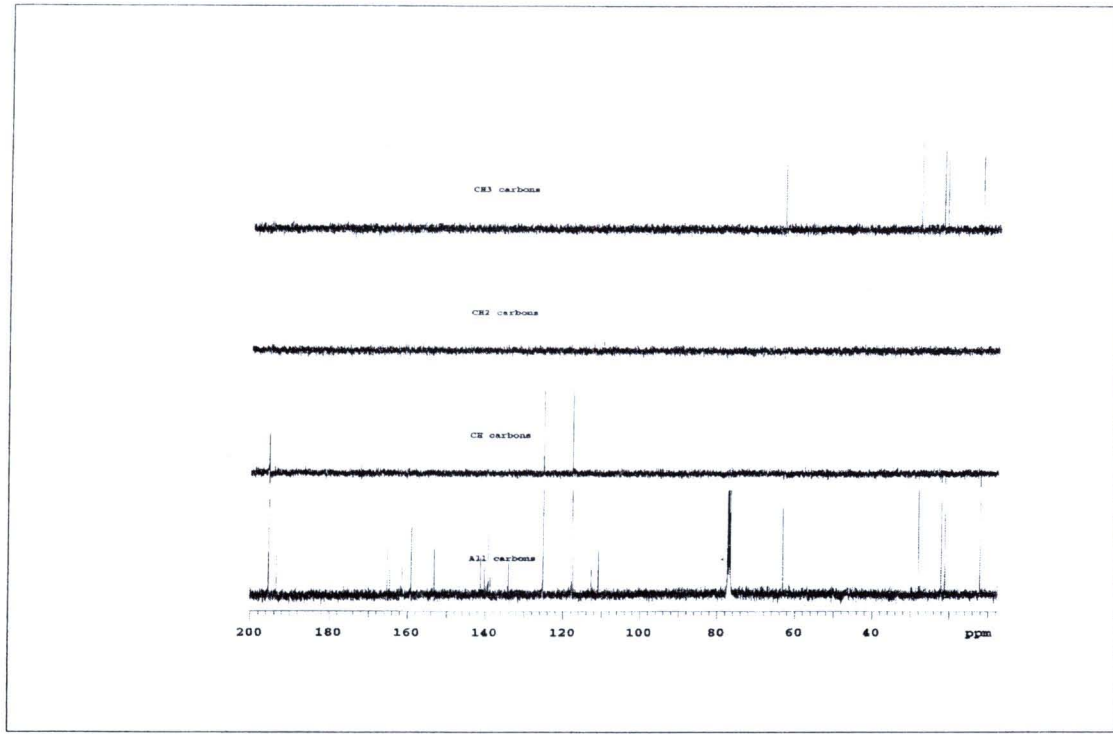

Figure 57 DEPT spectrum of mollicellin C **(1.9).**

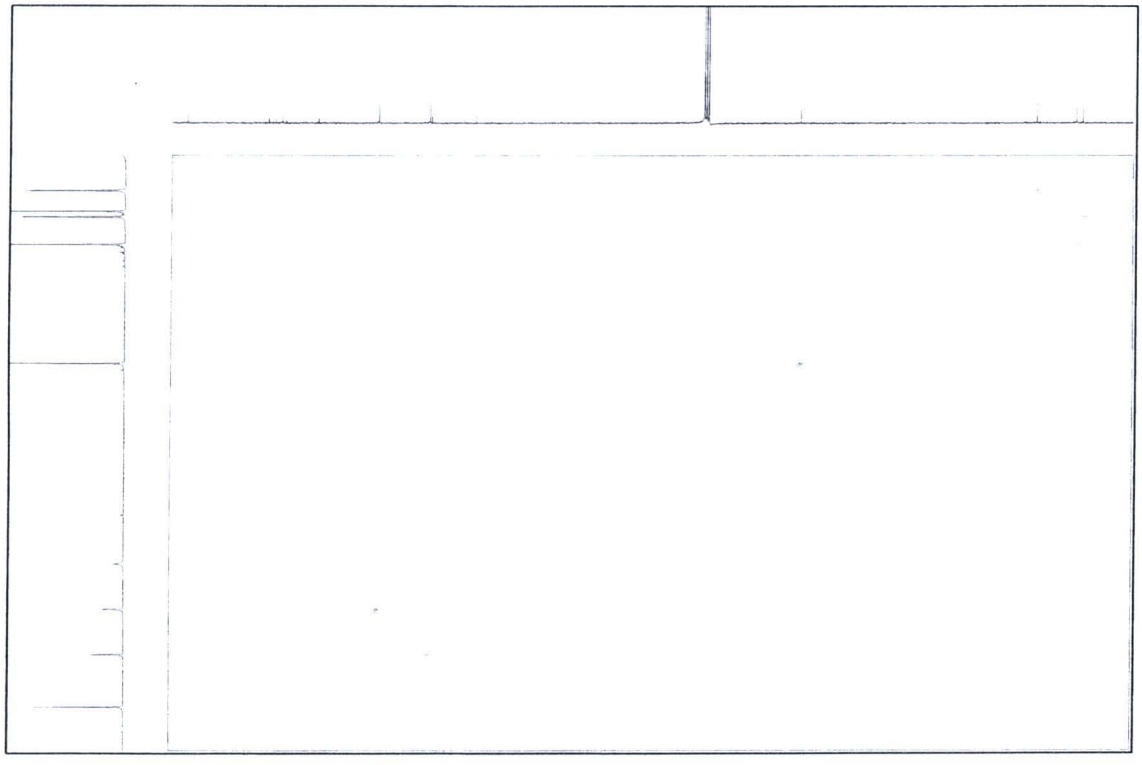

Figure 58 HSQC spectrum of mollicellin C **(1.9)**.

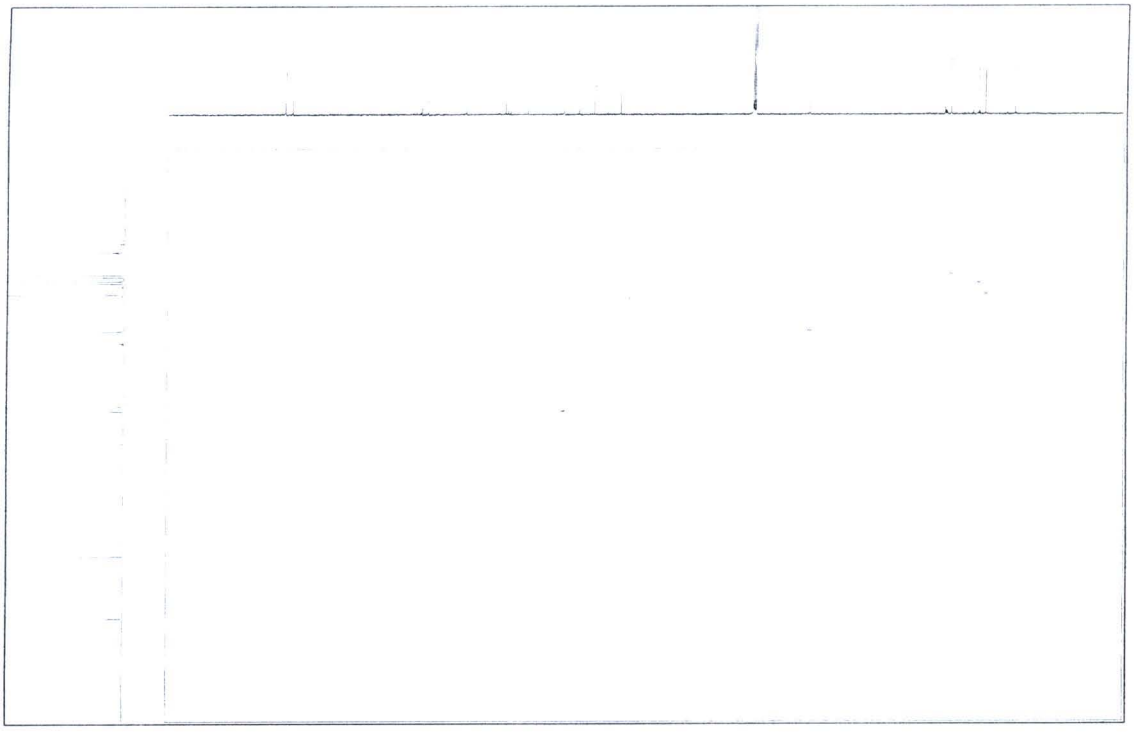

Figure 59 HMBC spectrum of mollicellin C **(1.9)**.

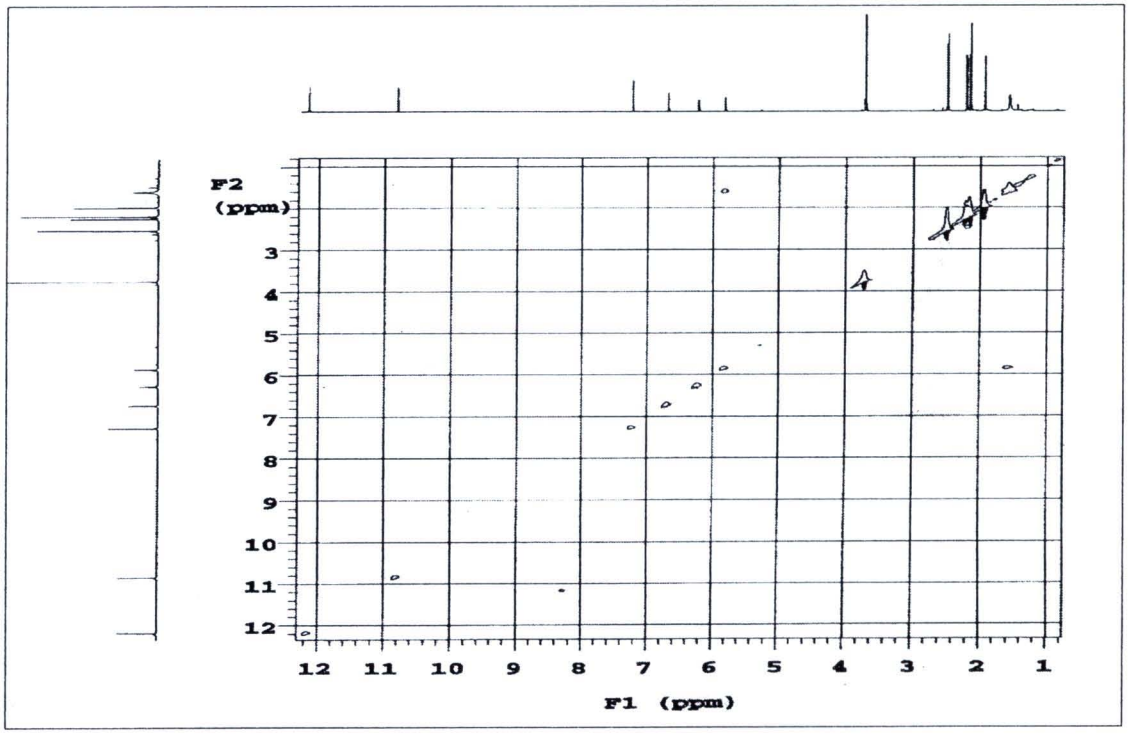

Figure 60 NOESY spectrum of mollicellin C **(1.9).**

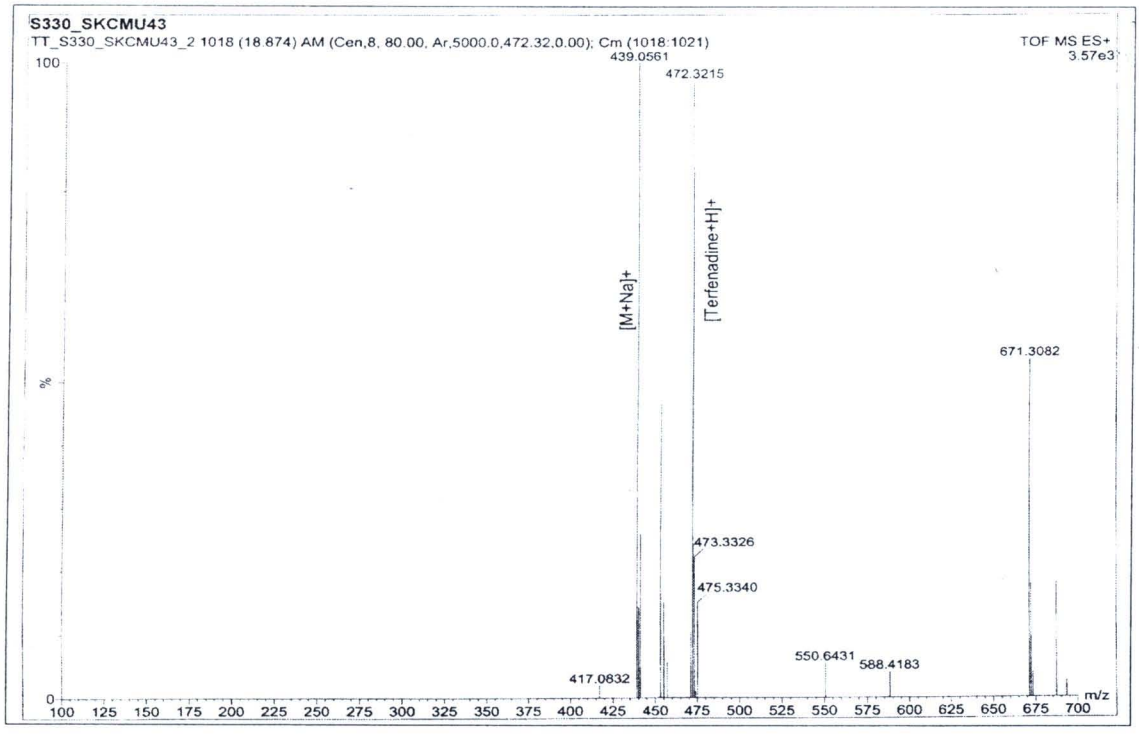

Figure 61 Mass spectrum of mollicellin E **(1.10).**

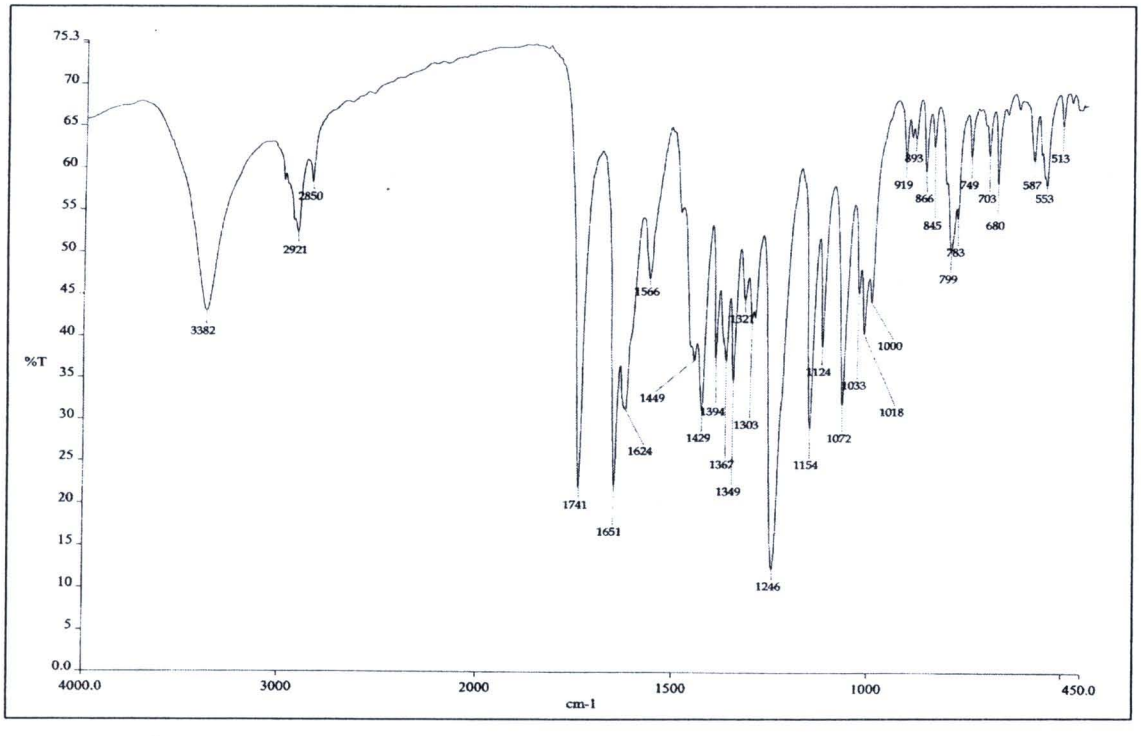

Figure 62 IR spectrum of mollicellin E **(1.10)**.

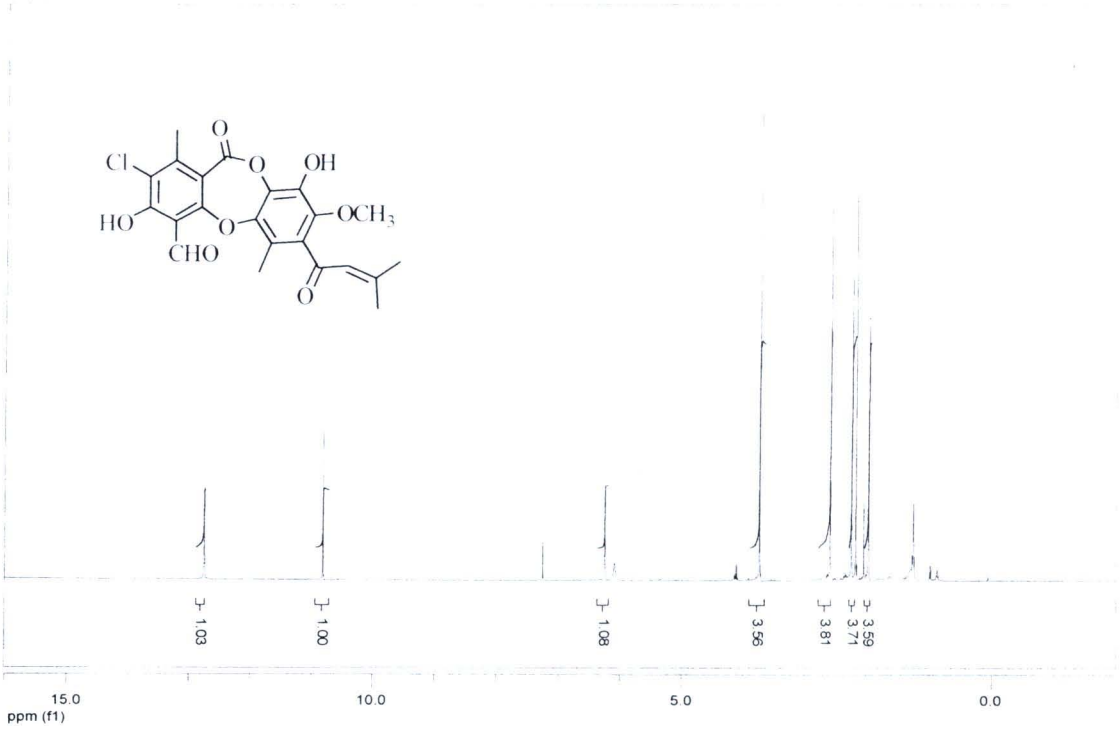

Figure 63 ^{1}H-NMR spectrum of mollicellin E **(1.10)**.

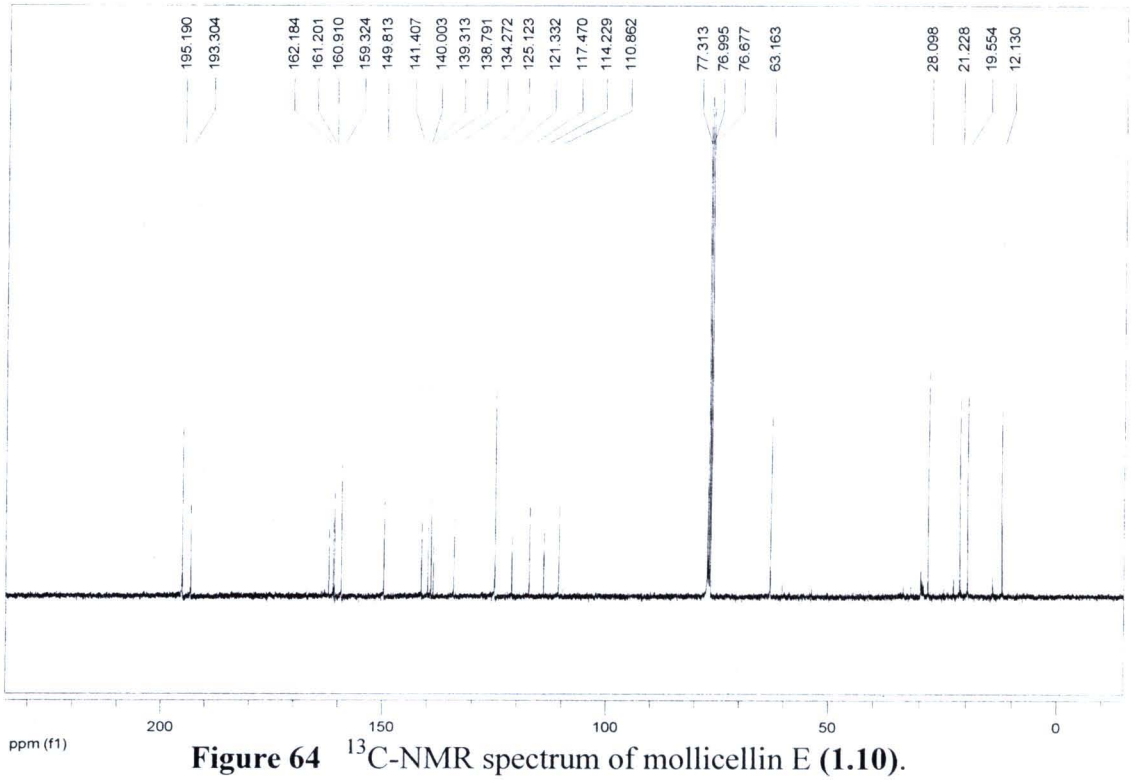

Figure 64 ^{13}C-NMR spectrum of mollicellin E **(1.10)**.

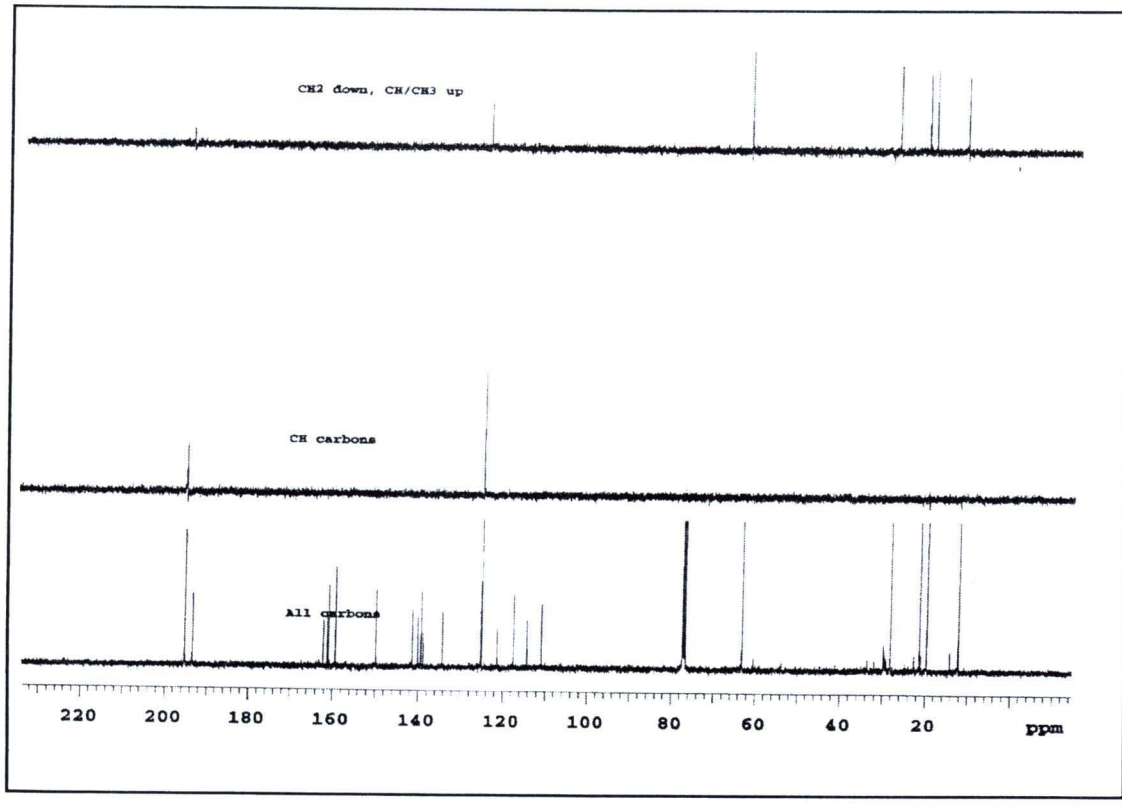

Figure 65 DEPT spectrum of mollicellin E **(1.10)**.

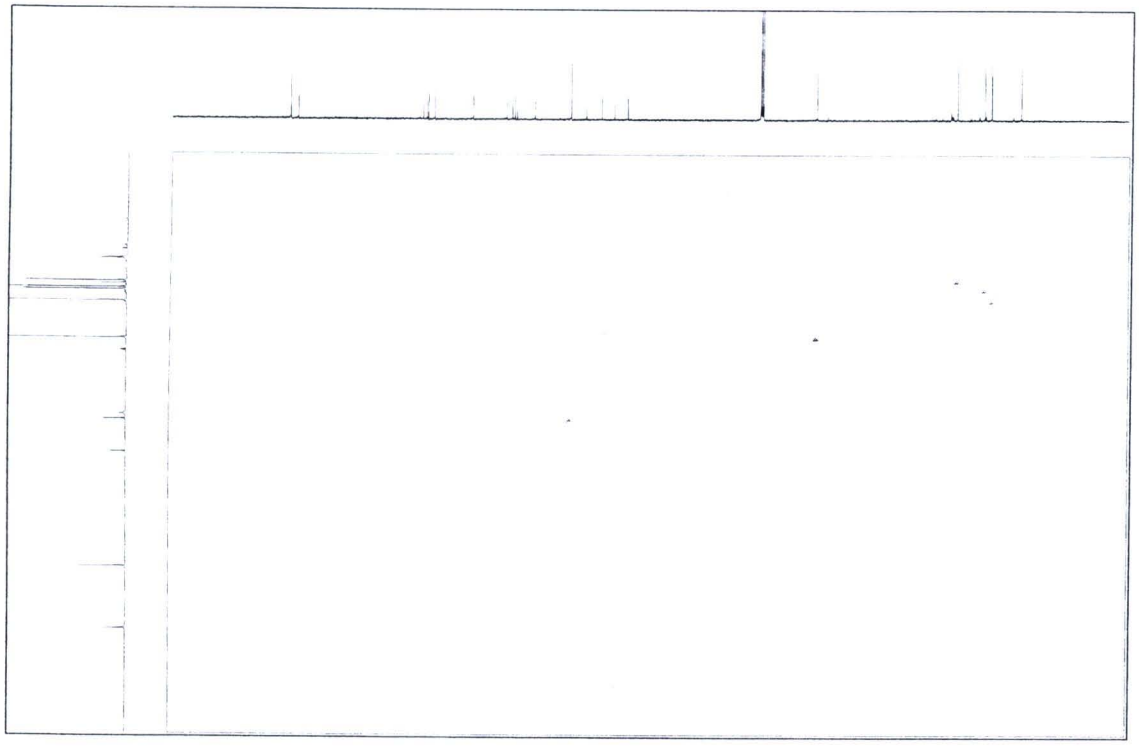

Figure 66 HSQC spectrum of mollicellin E **(1.10)**.

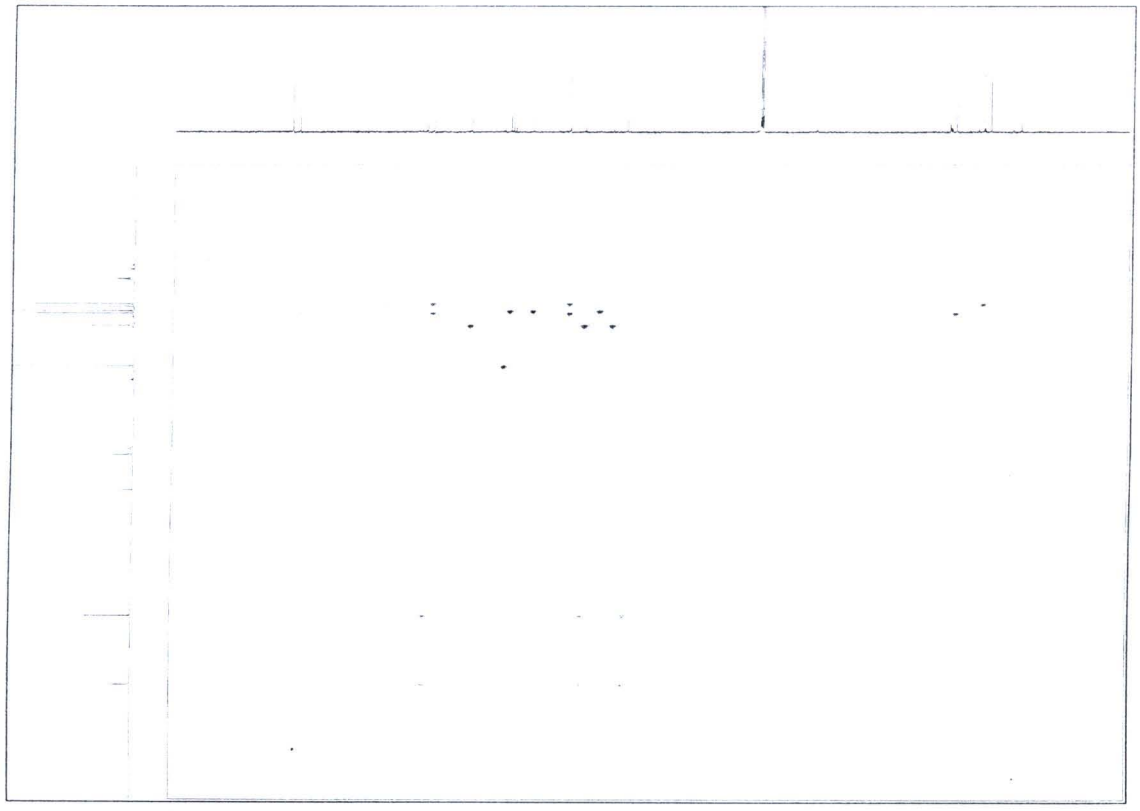

Figure 67 HMBC spectrum of mollicellin E **(1.10).**

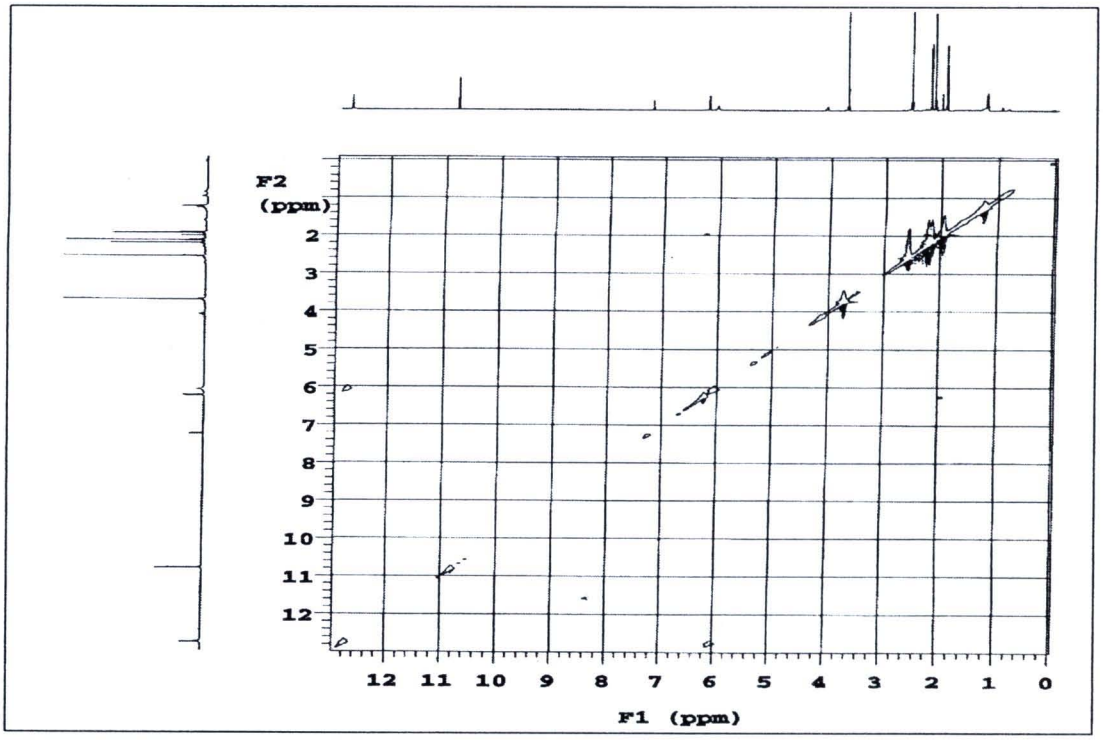

Figure 68 NOSEY spectrum of mollicellin E **(1.10)**.

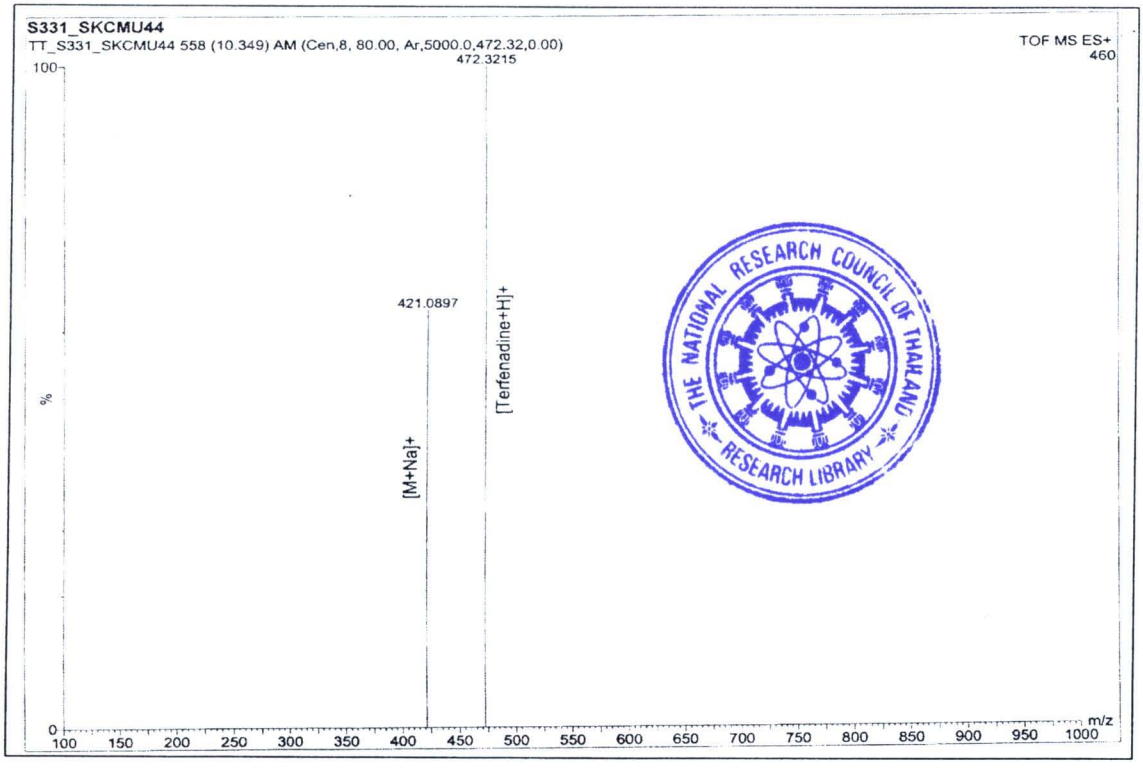

Figure 69 Mass spectrum of mollicellin N **(1.11)**.

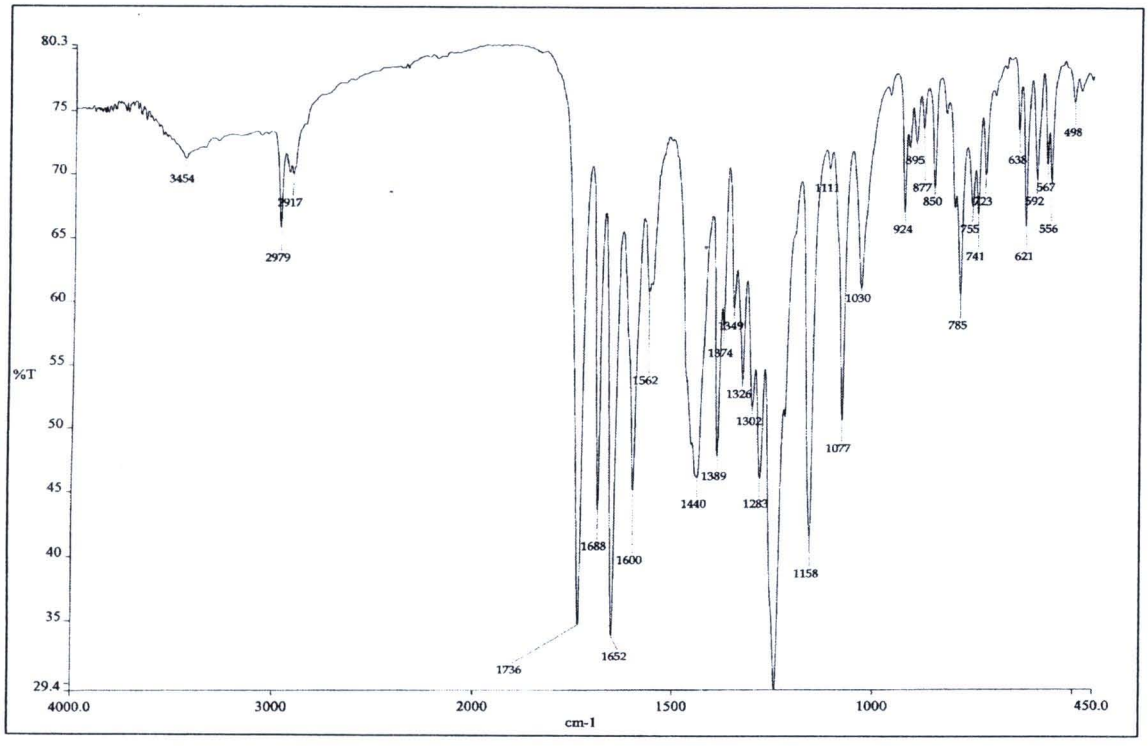

Figure 70 IR spectrum of mollicellin N **(1.11)**.

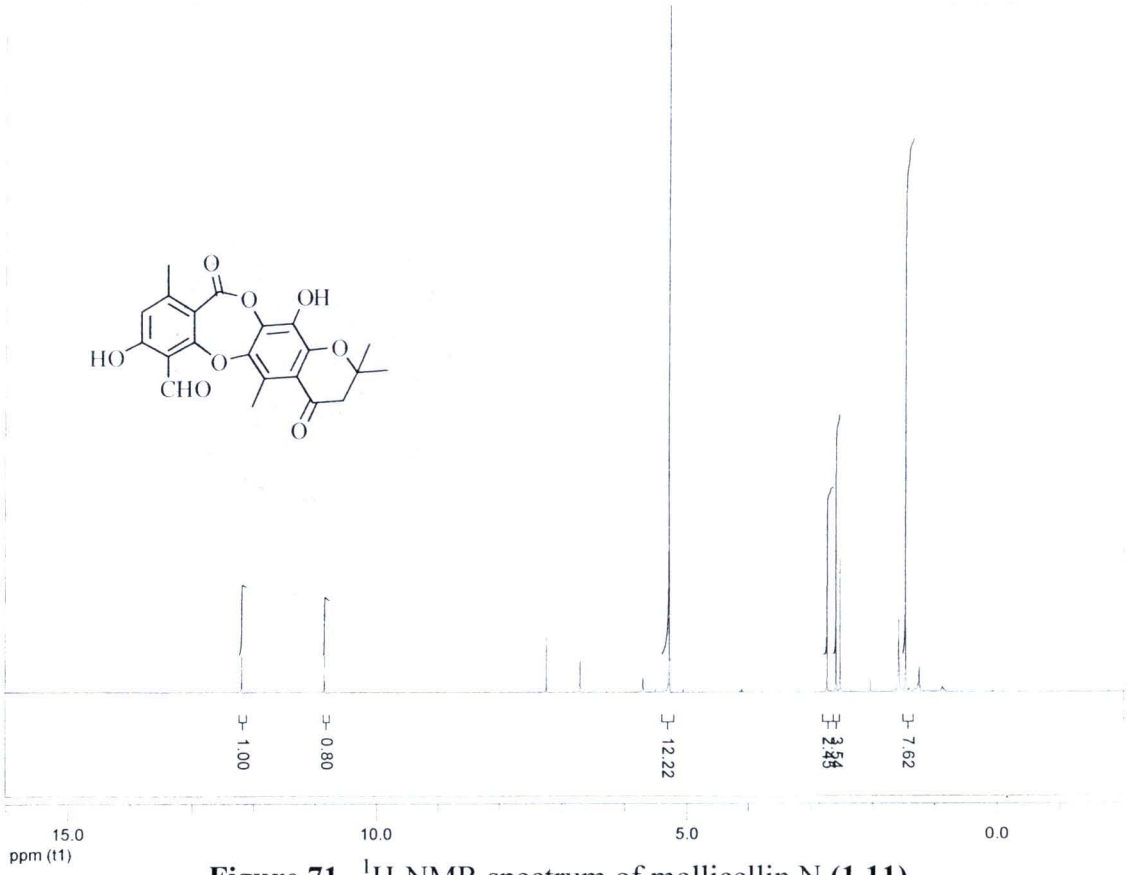

Figure 71 ^{1}H-NMR spectrum of mollicellin N **(1.11)**.

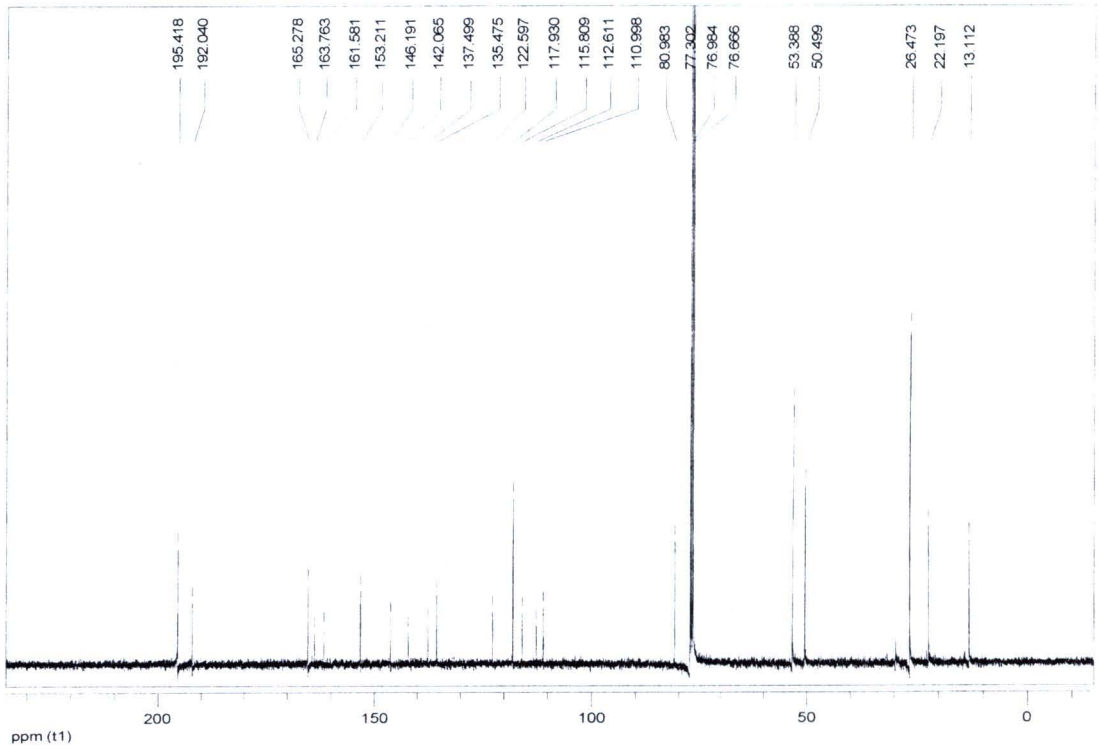

Figure 72 ^{13}C-NMR spectrum of mollicellin N **(1.11)**.

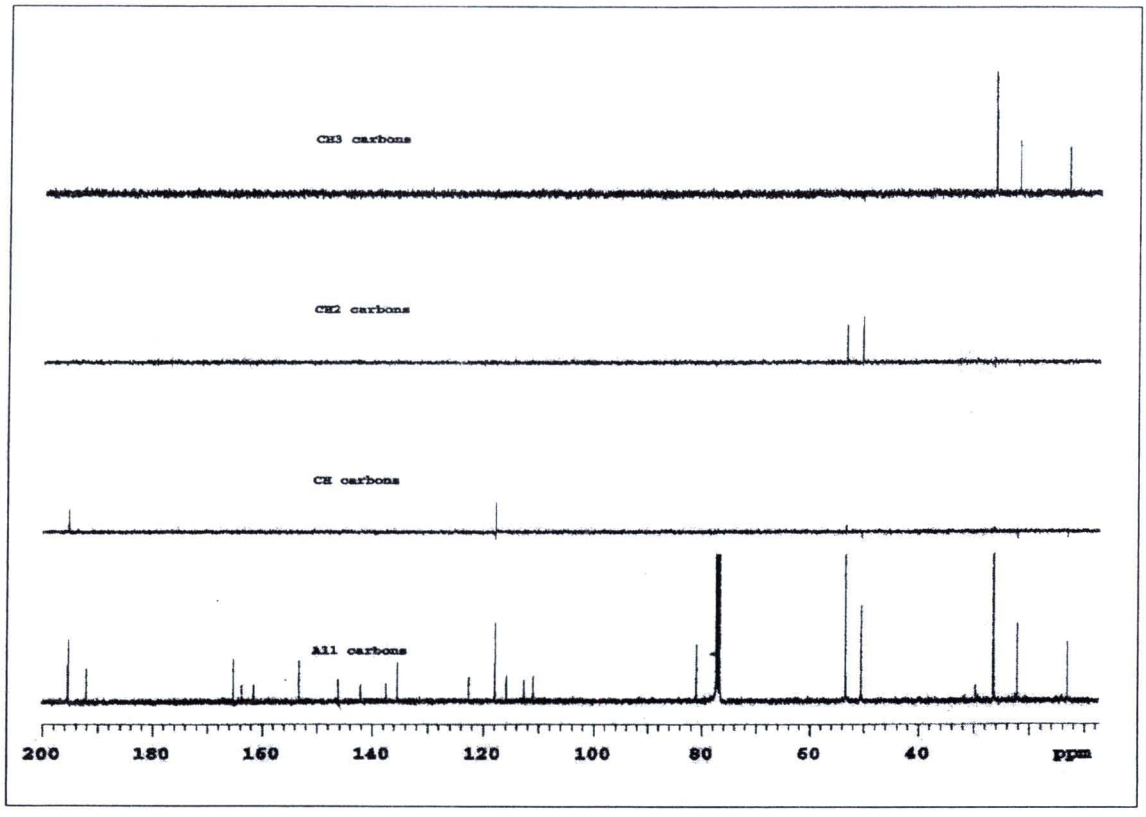

Figure 73 DEPT spectrum of mollicellin N **(1.11)**.

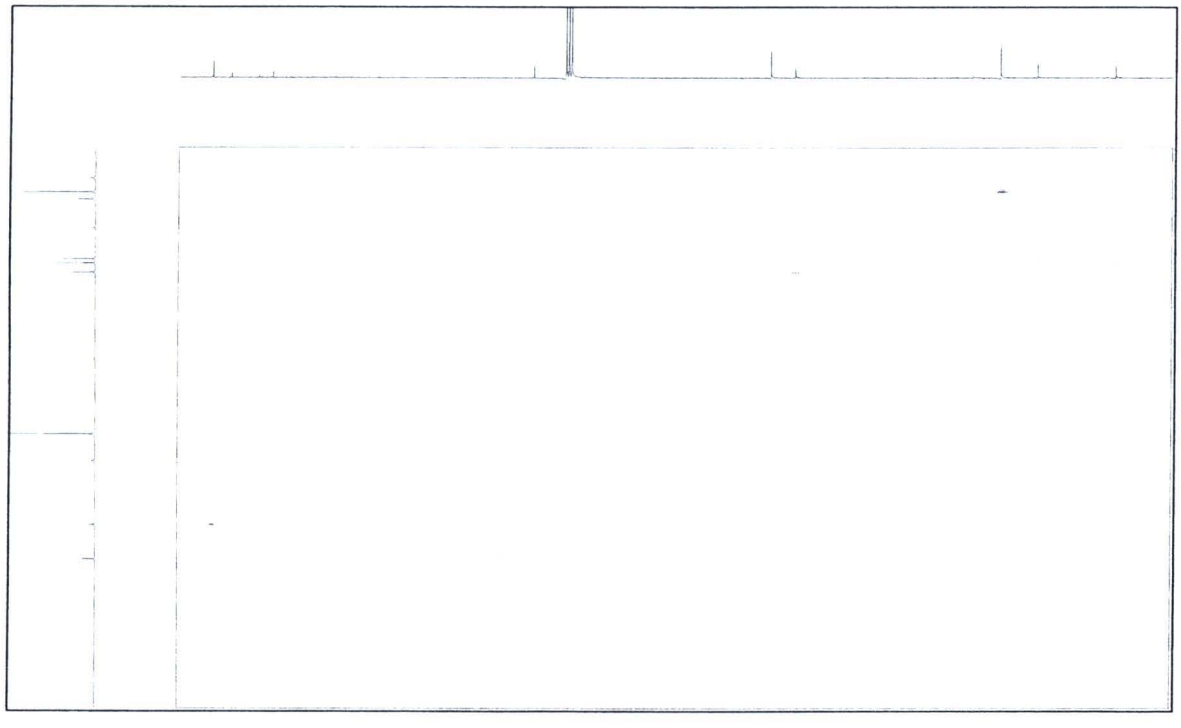

Figure 74 HSQC spectrum of mollicellin N **(1.11)**.

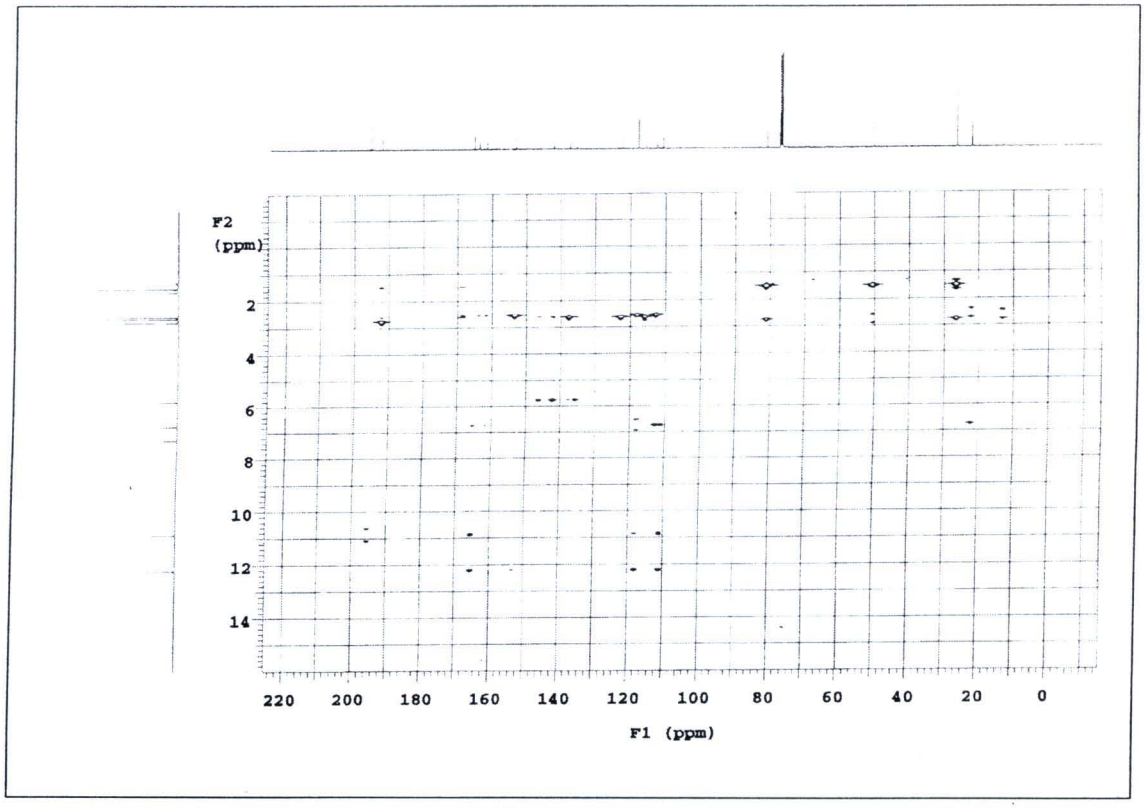

Figure 75 HMBC spectrum of mollicellin N **(1.11)**

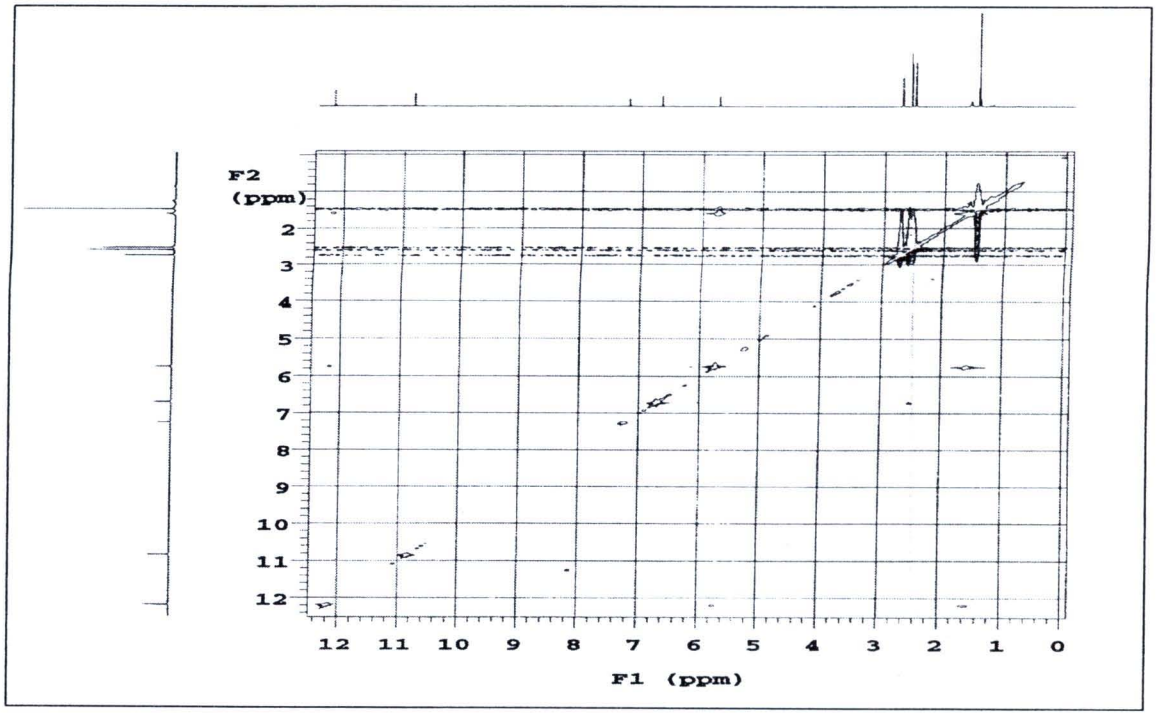

Figure 76 NOESY spectrum of mollicellin N **(1.11)**.

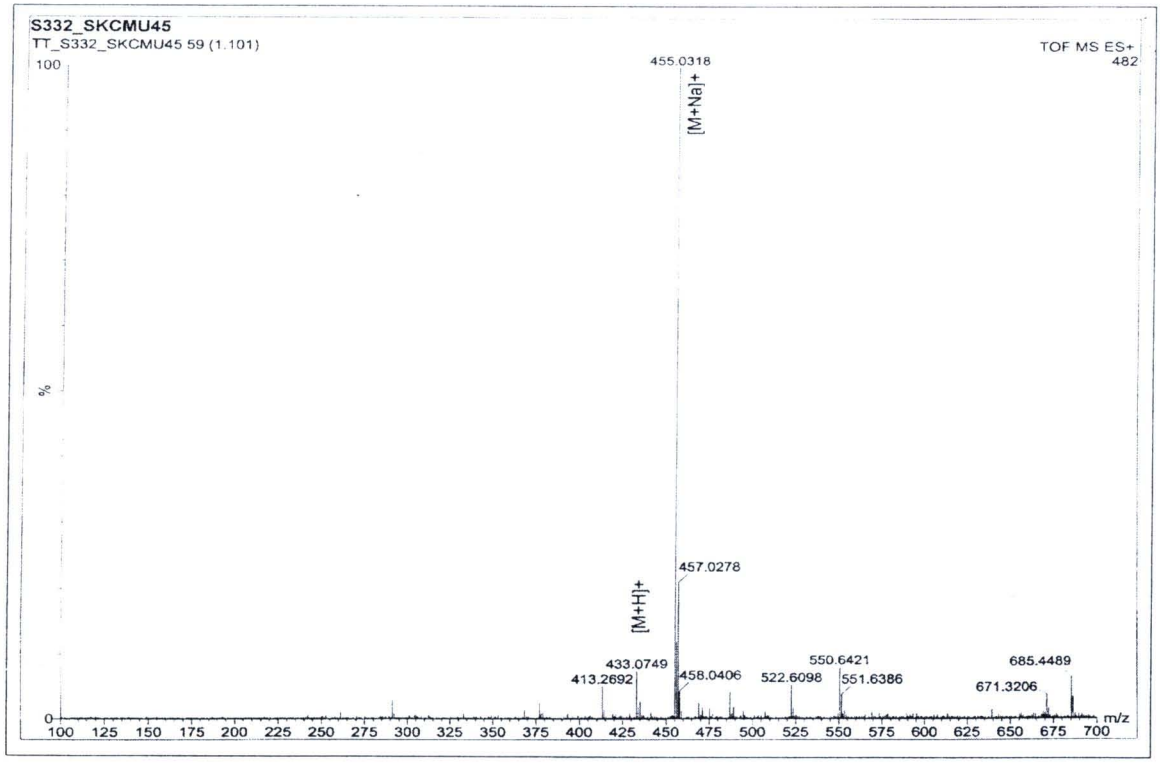

Figure 77 Mass spectrum of mollicellin F **(1.12)**.

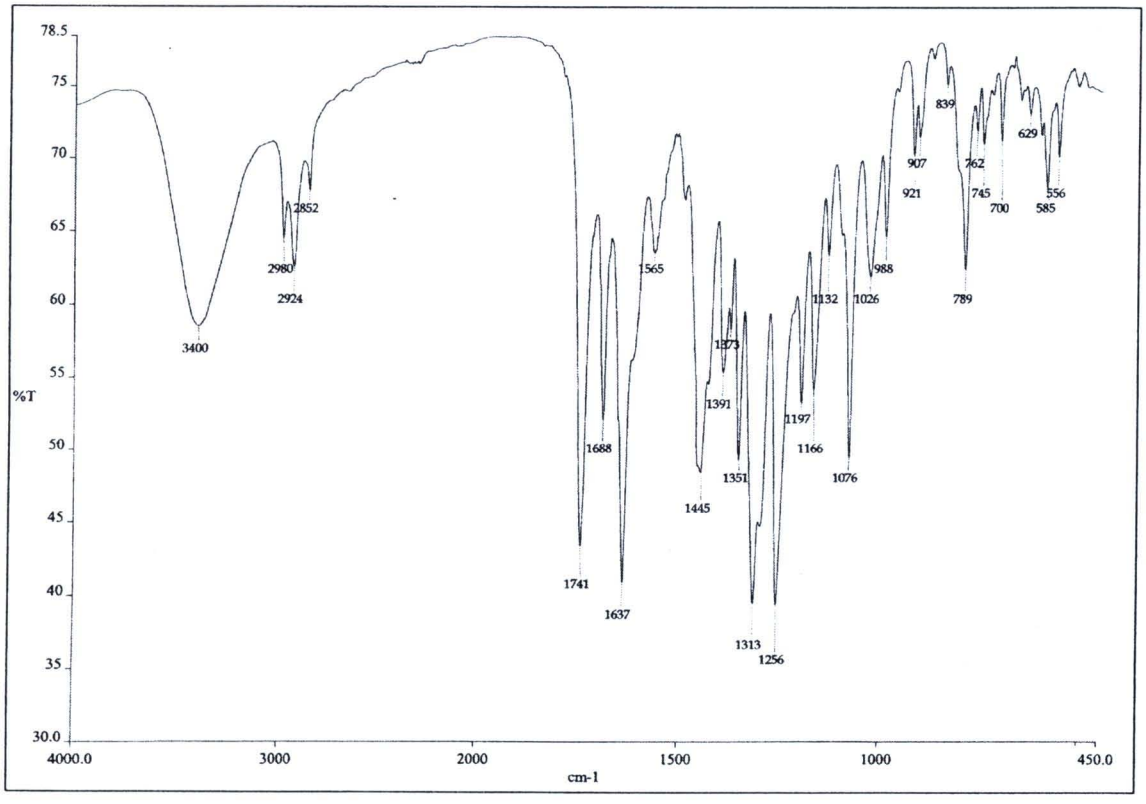

Figure 78 IR spectrum of mollicellin F **(1.12)**.

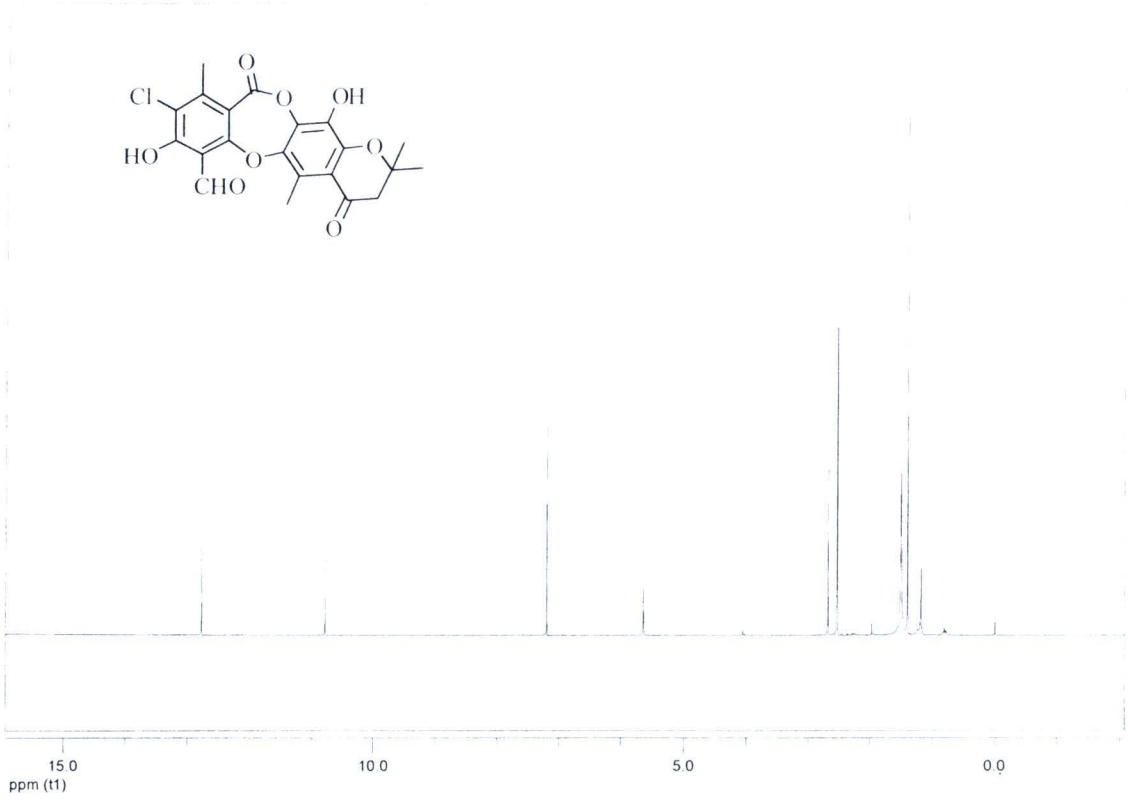

Figure 79 ^{1}H-NMR spectrum of mollicellin F **(1.12)**

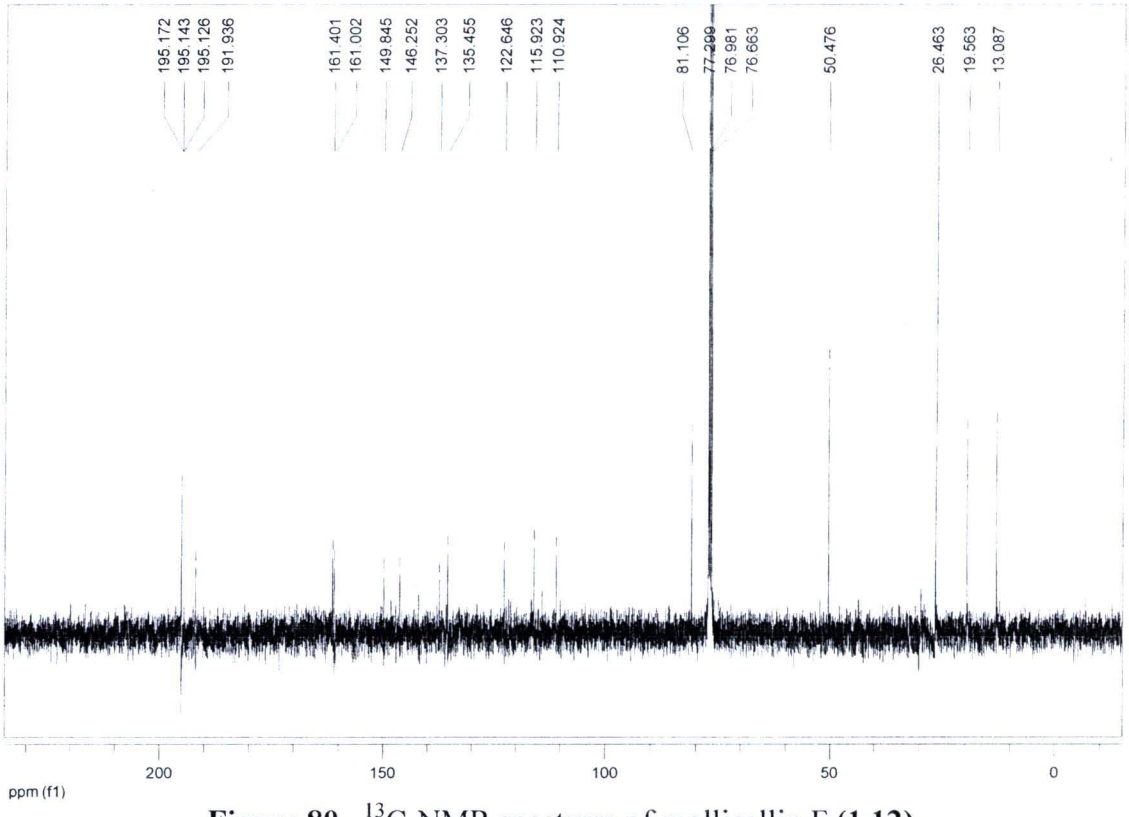

Figure 80 ^{13}C-NMR spectrum of mollicellin F **(1.12)**.

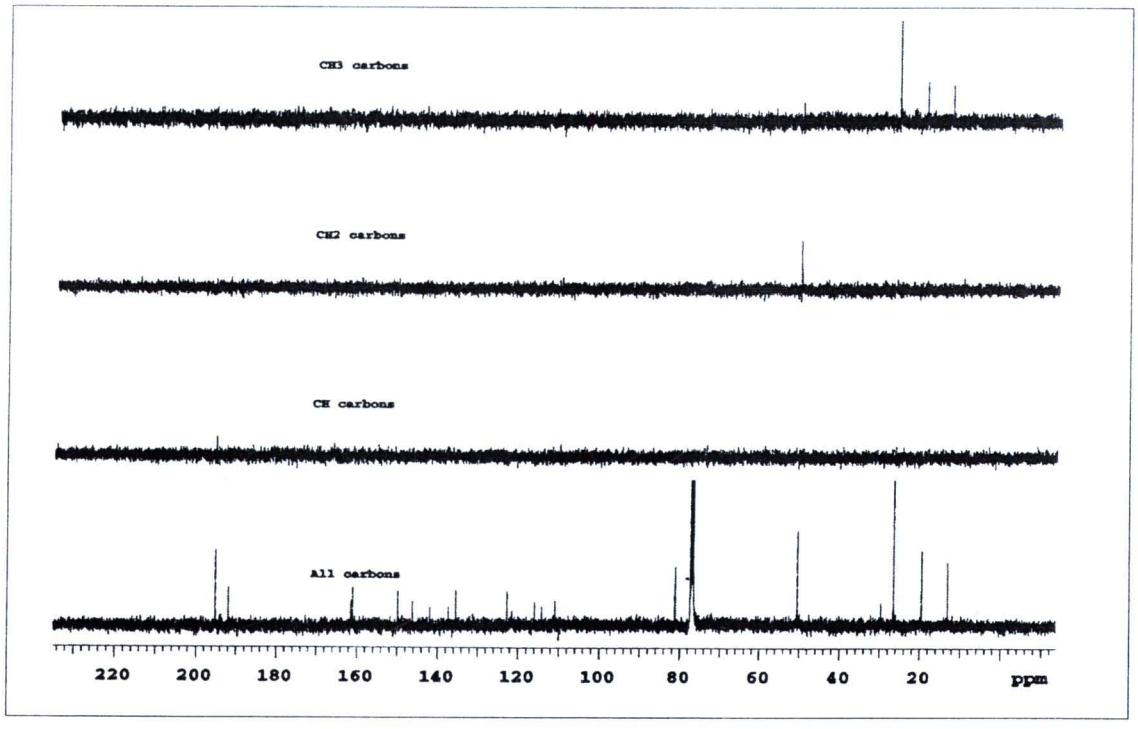

Figure 81 DEPT spectrum of mollicellin F **(1.12)**)

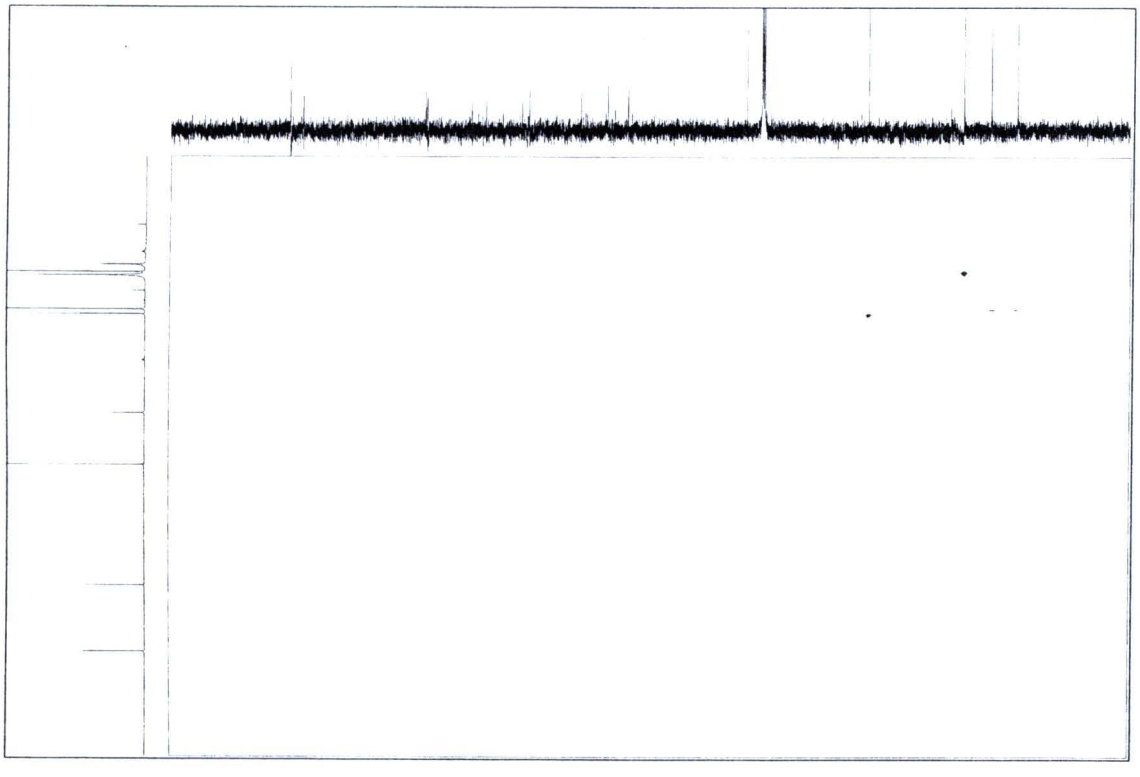

Figure 82 HSQC spectrum of mollicellin F **(1.12)**.

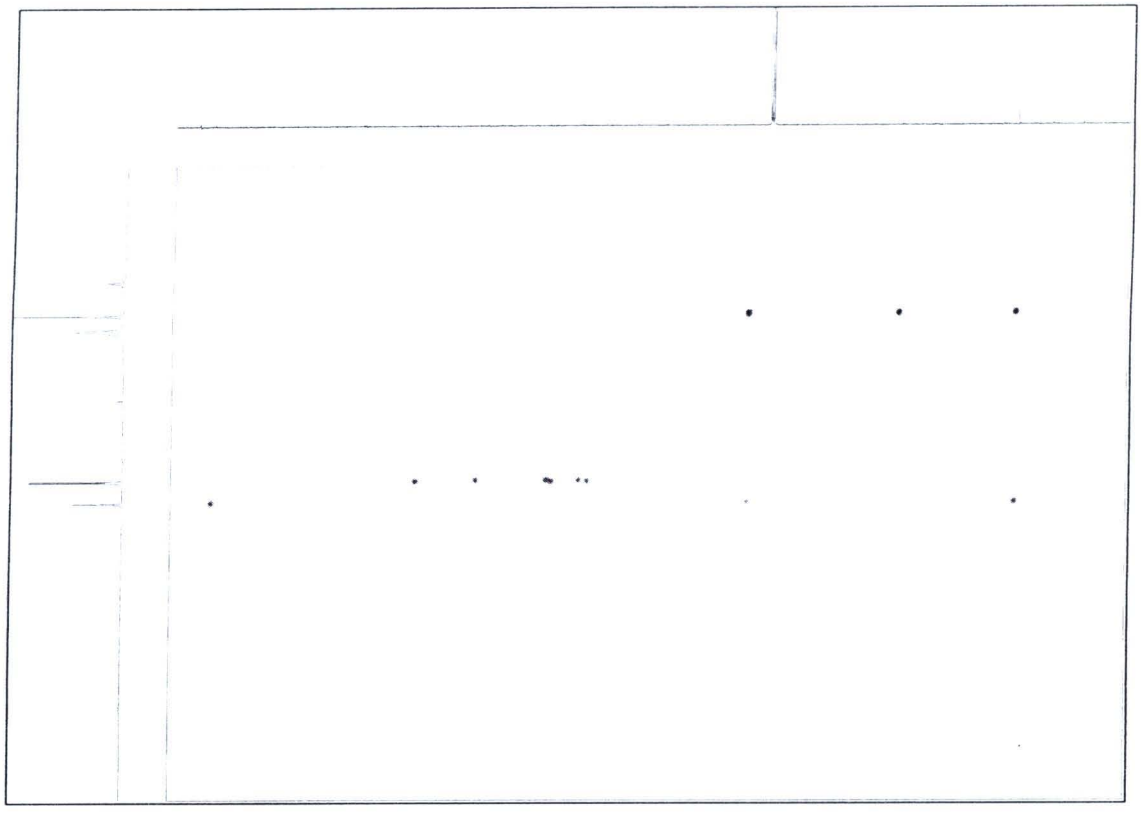

Figure 83 HMBC spectrum of mollicellin F **(1.12)**.

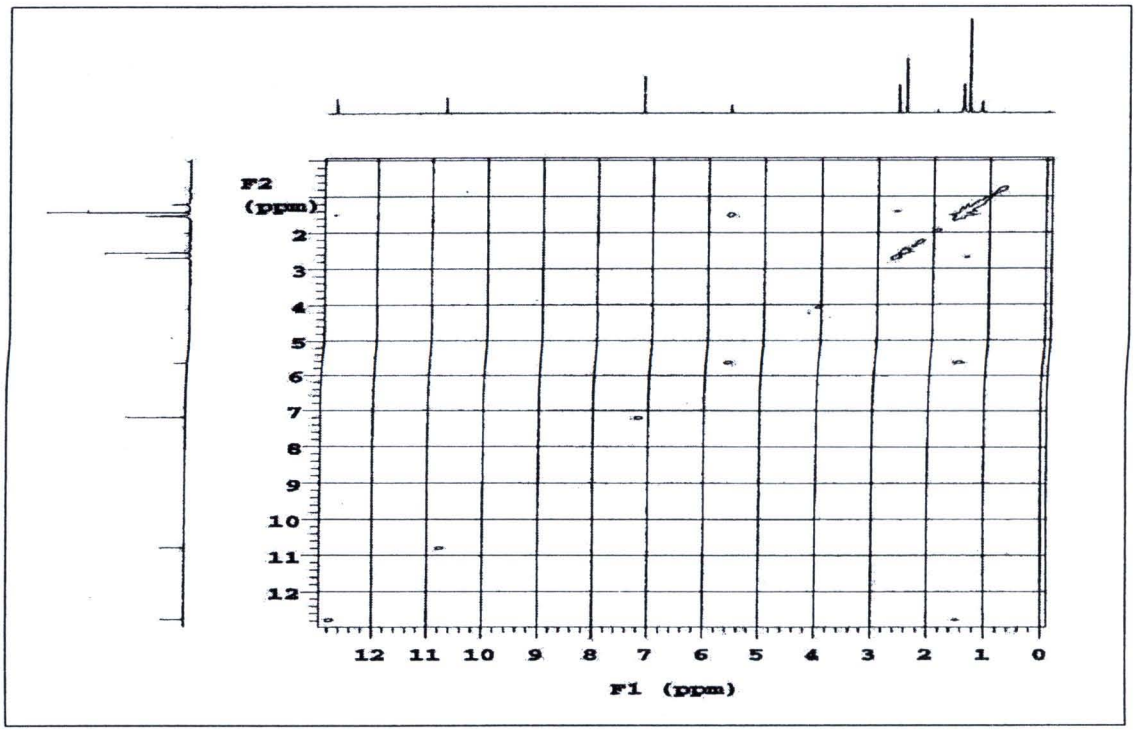

Figure 84 NOSEY spectrum of mollicellin F **(1.12)**.

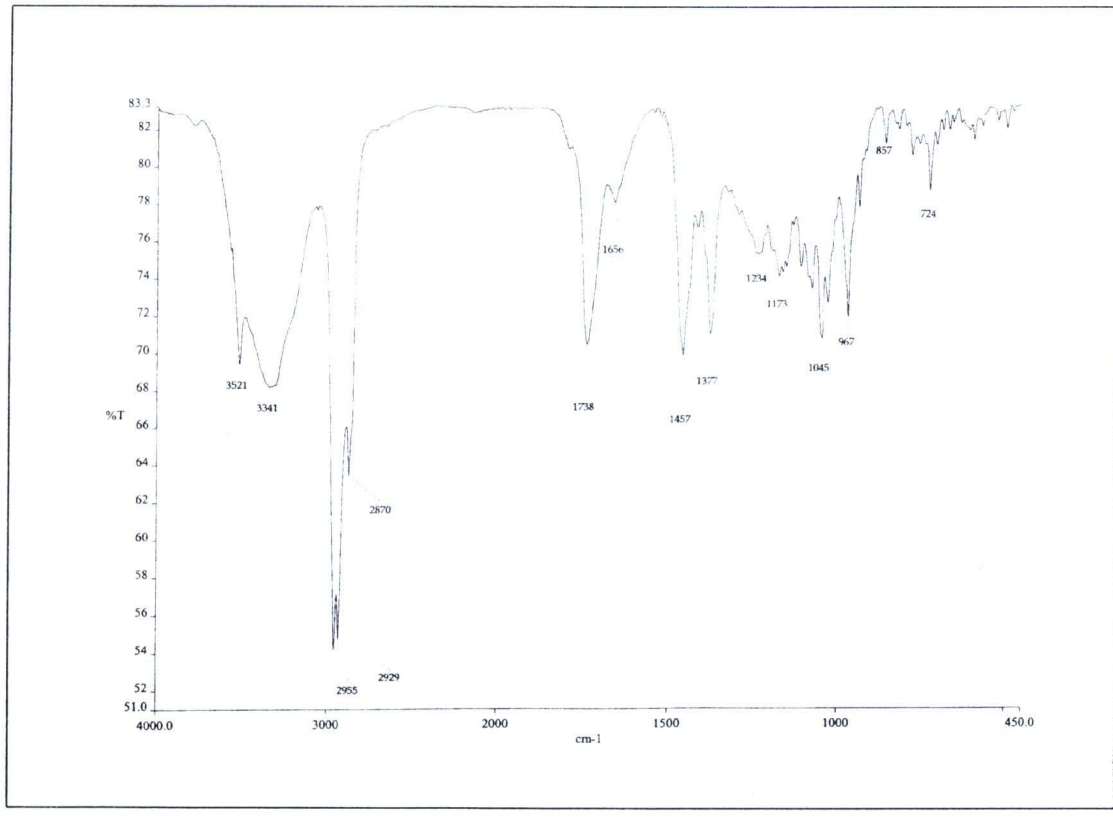

Figure 85 IR spectrum of ergosterylplamitate **(2.3** or **3.3)**.

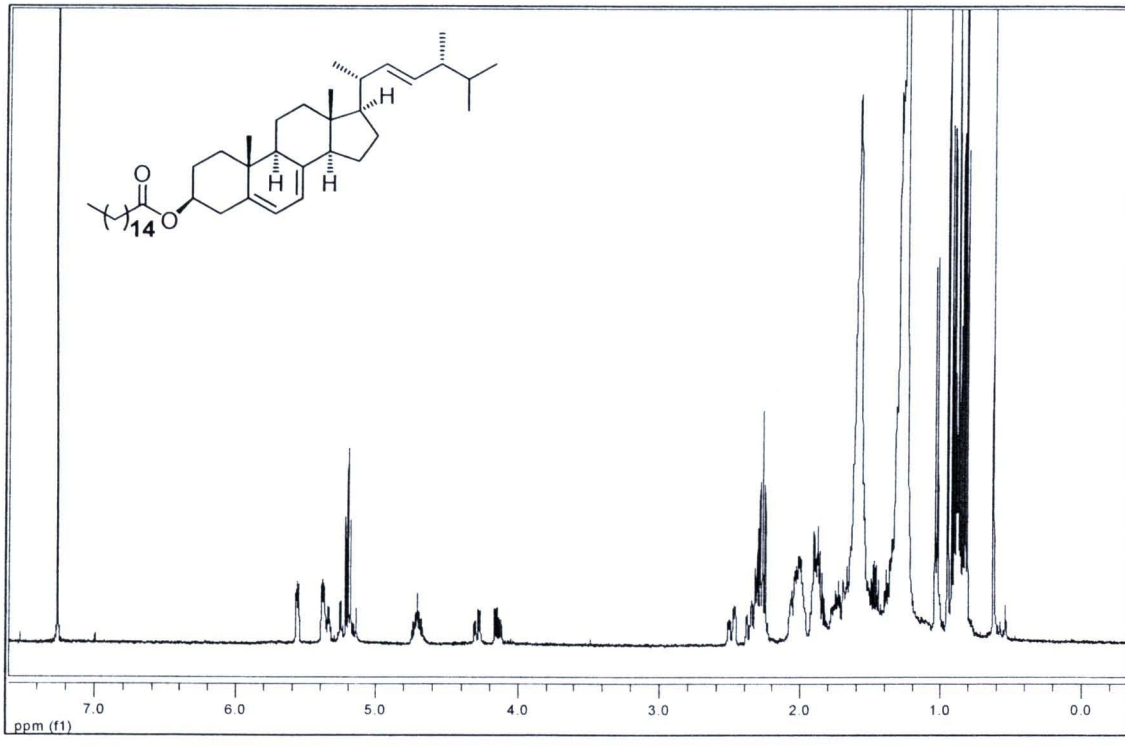

Figure 86 ^{1}H-NMR spectrum of ergosterylplamitate **(2.3** or **3.3)**.

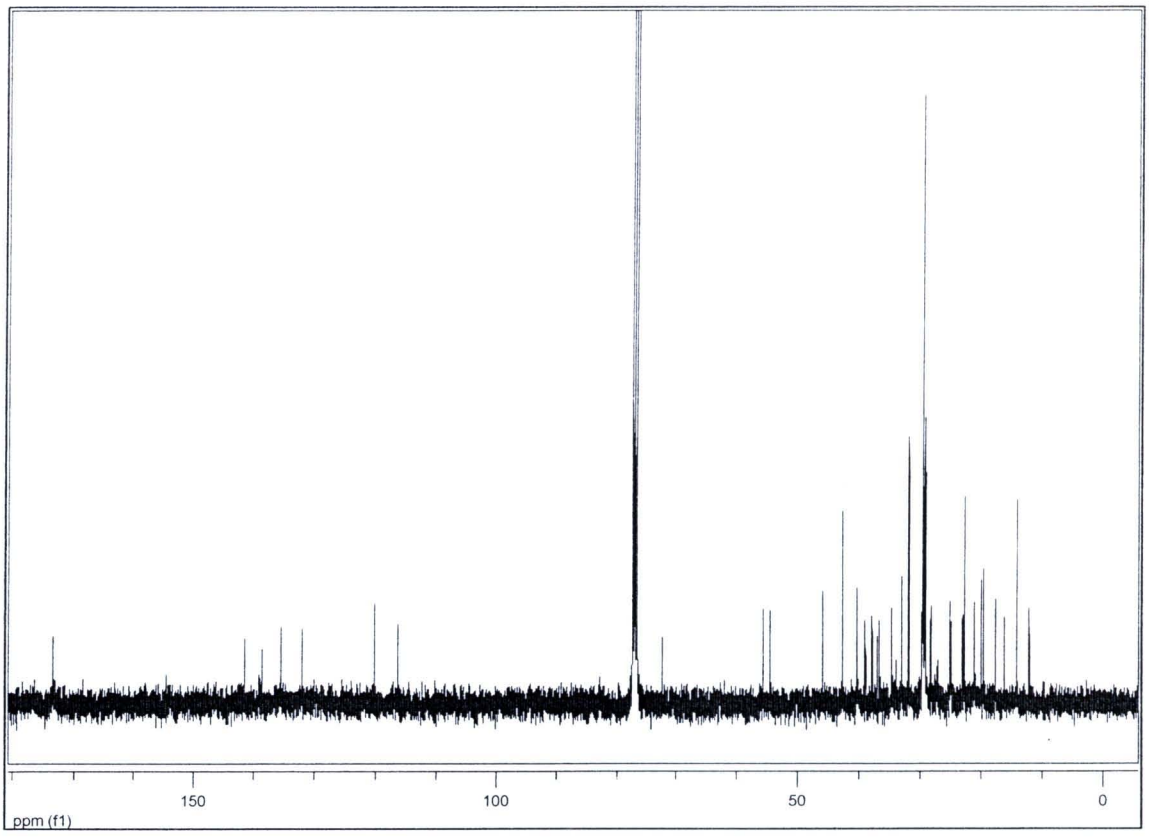

Figure 87 ^{13}C-NMR spectrum of ergosterylplamitate (**2.3** or **3.3**)

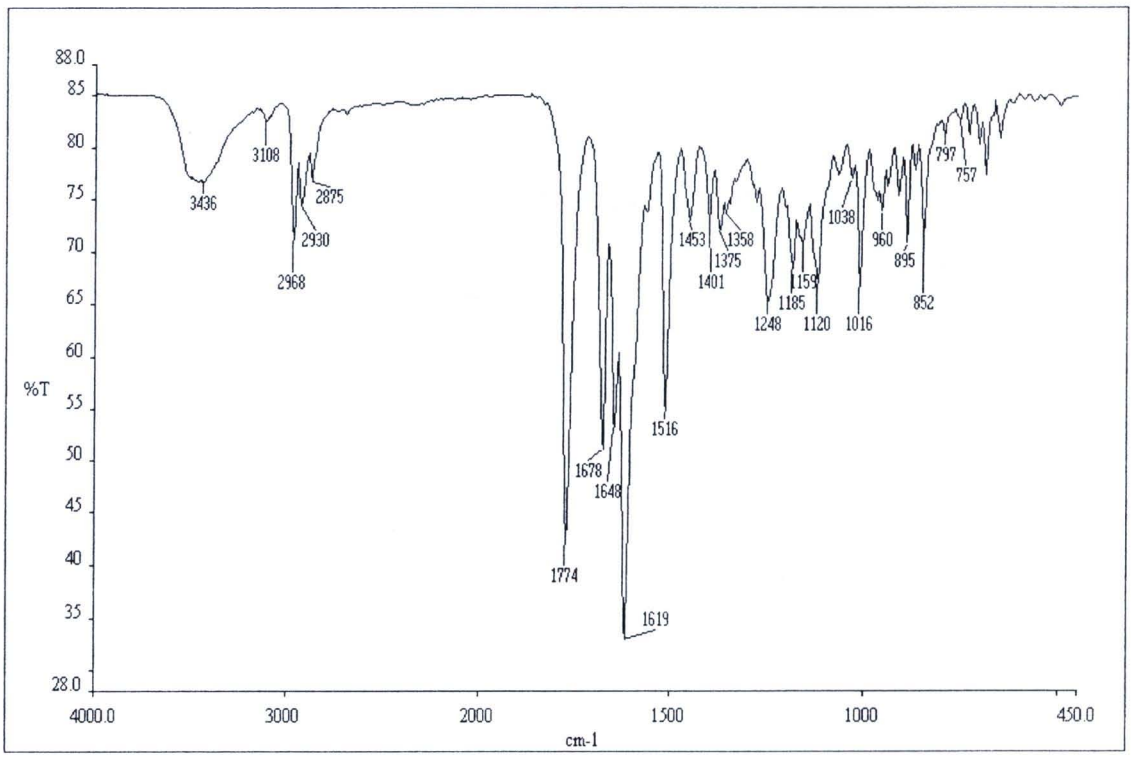

Figure 88 IR spectrum of chaetoviridin A (**2.4**).

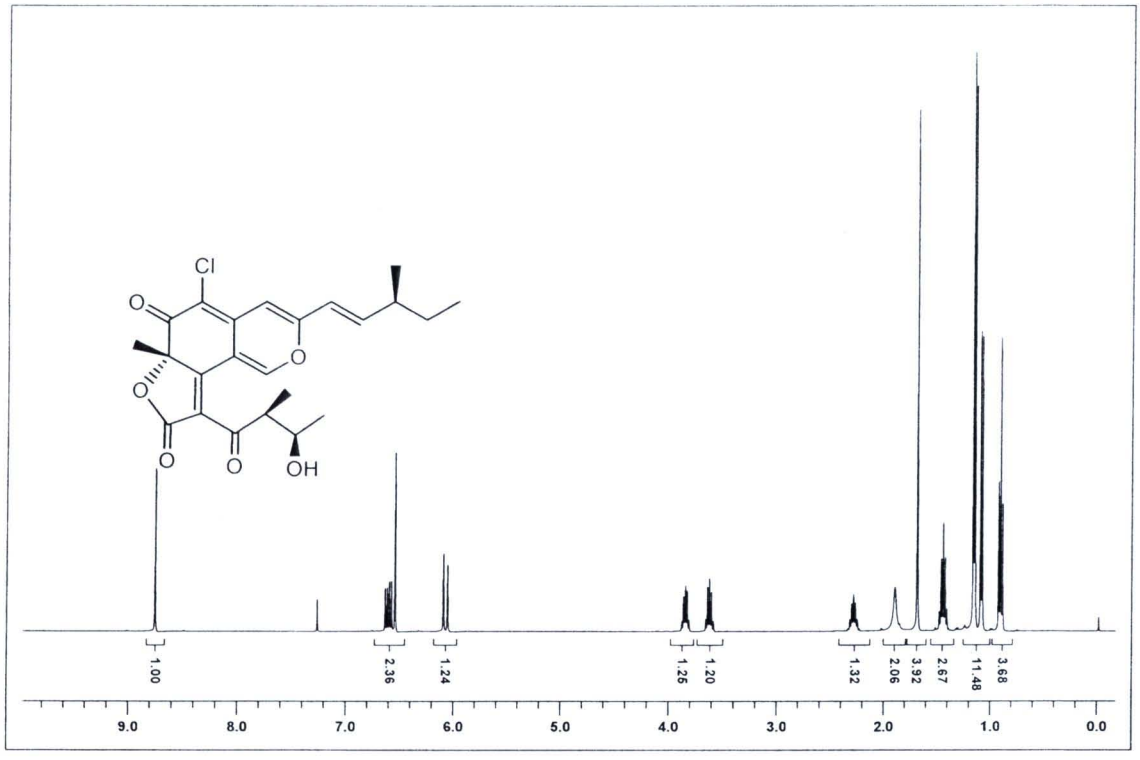

Figure 89 ^{1}H NMR spectrum of chaetoviridin A (**2.4**).

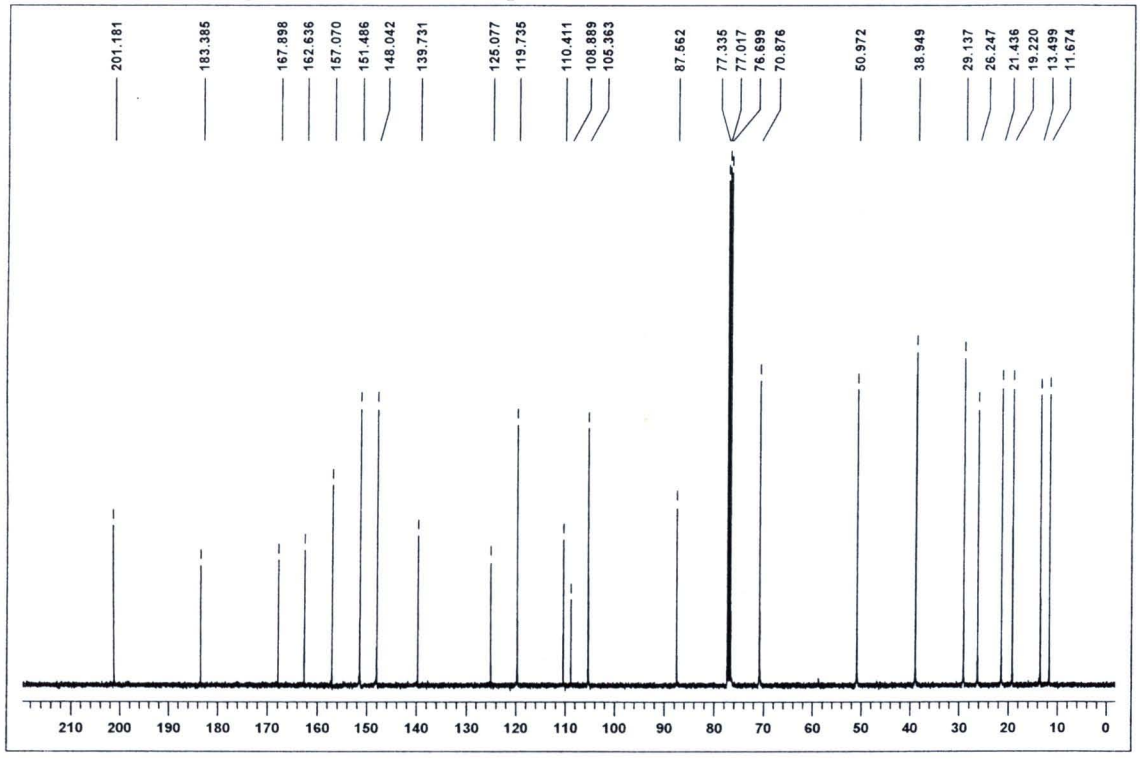

Figure 90 ^{13}C NMR spectrum of chaetoviridin A (**2.4**).

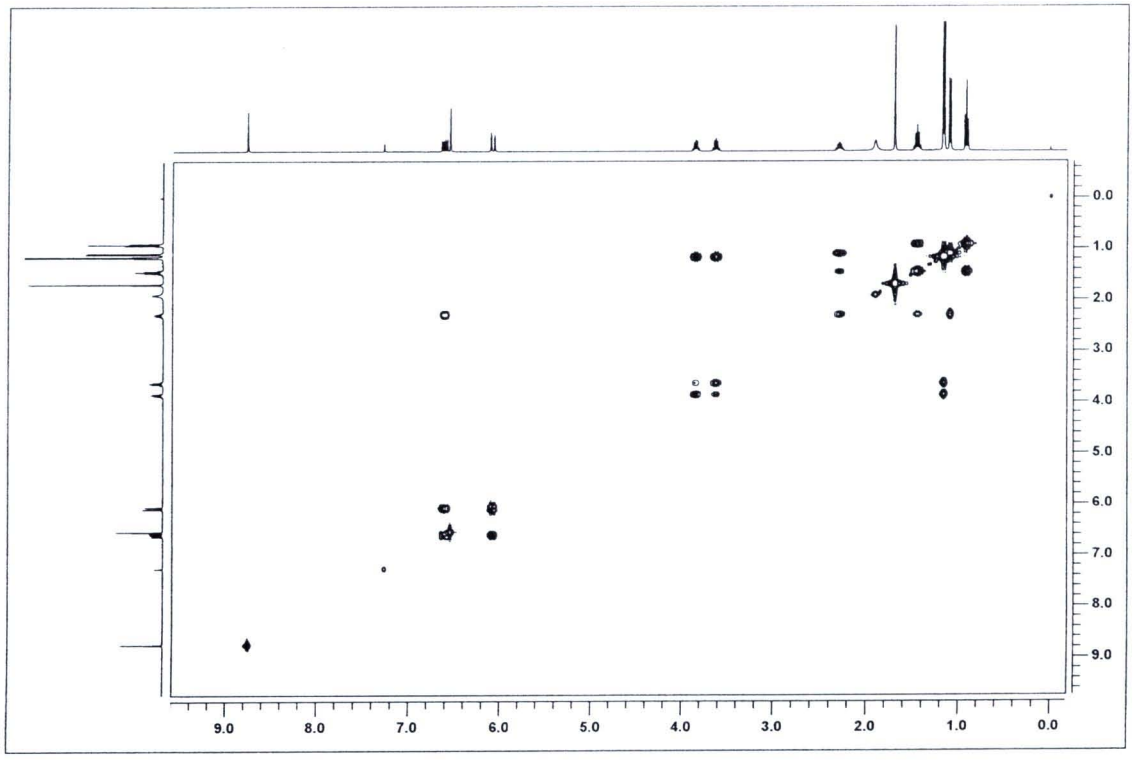

Figure 91 COSY spectrum of chaetoviridin A (**2.4**).

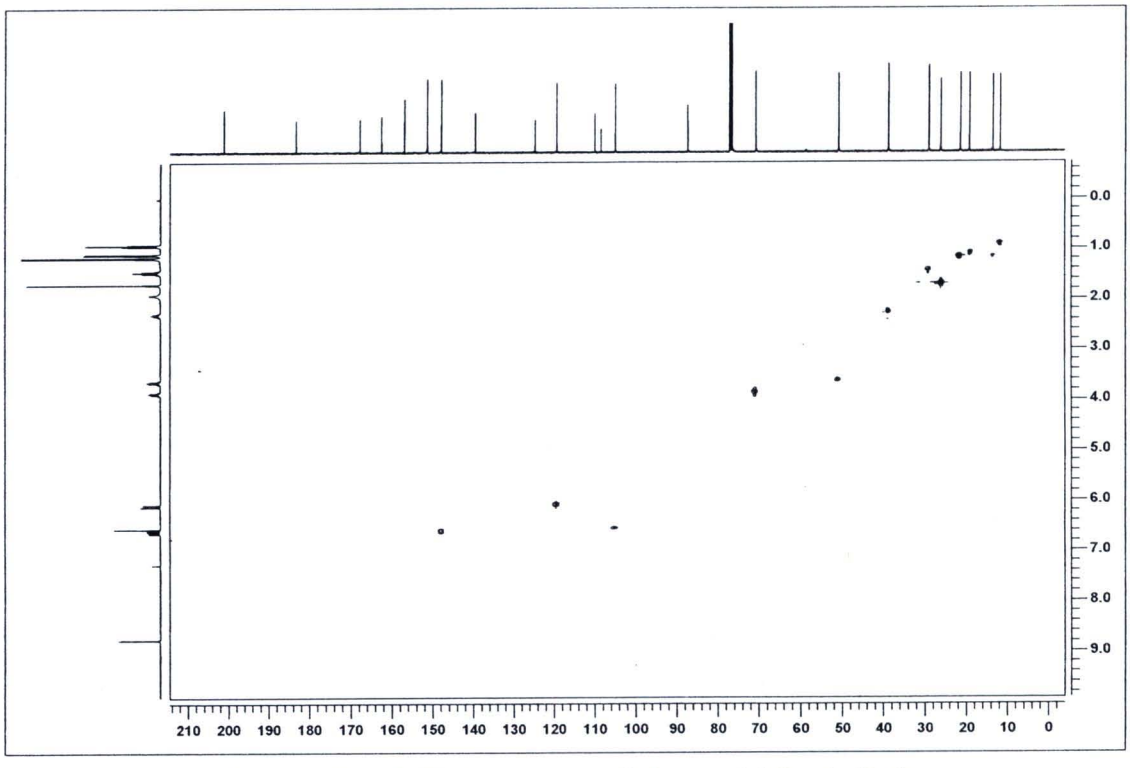

Figure 92 HSQC spectrum of chaetoviridin A (**2.4**).

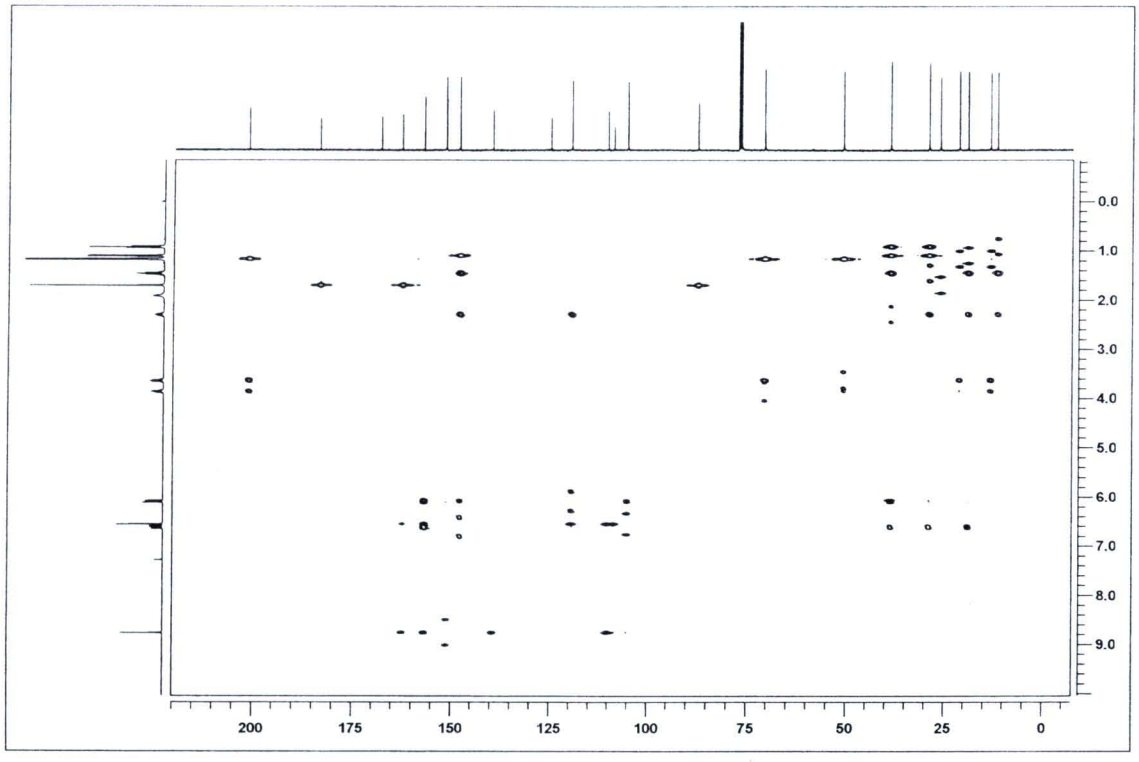

Figure 93 HMBC spectrum of chaetoviridin A (**2.4**).

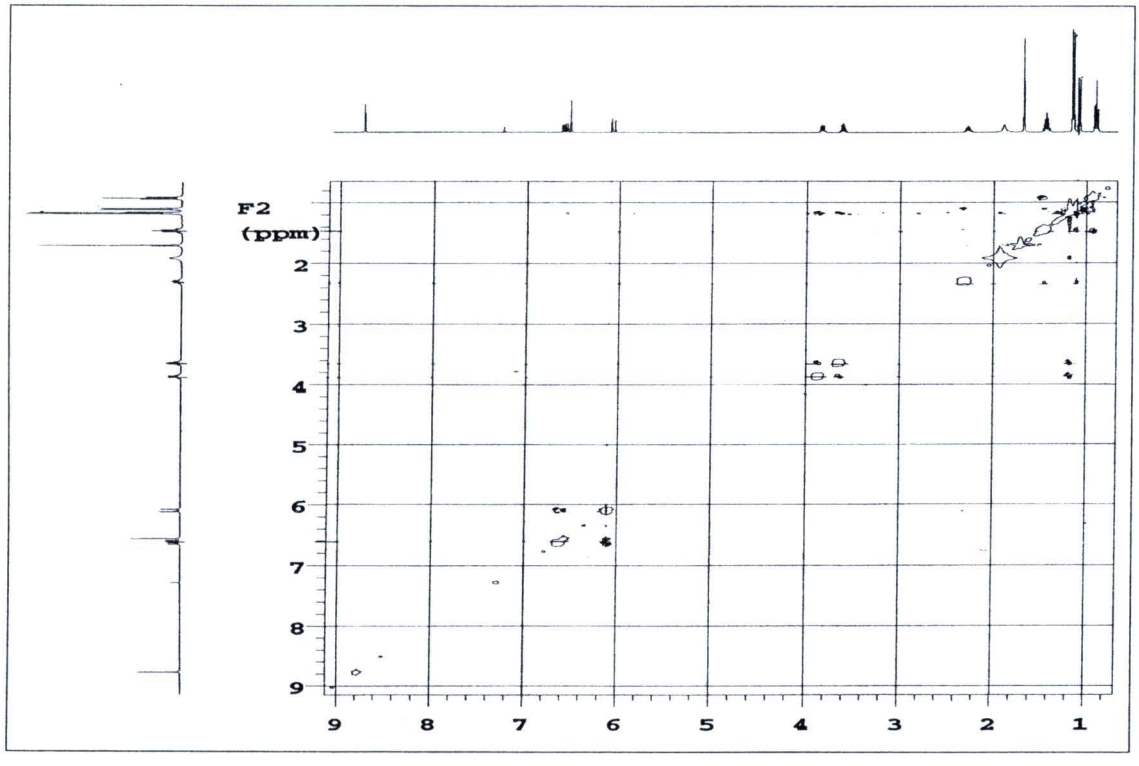

Figure 94 NOESY spectrum of chaetoviridin A (**2.4**).

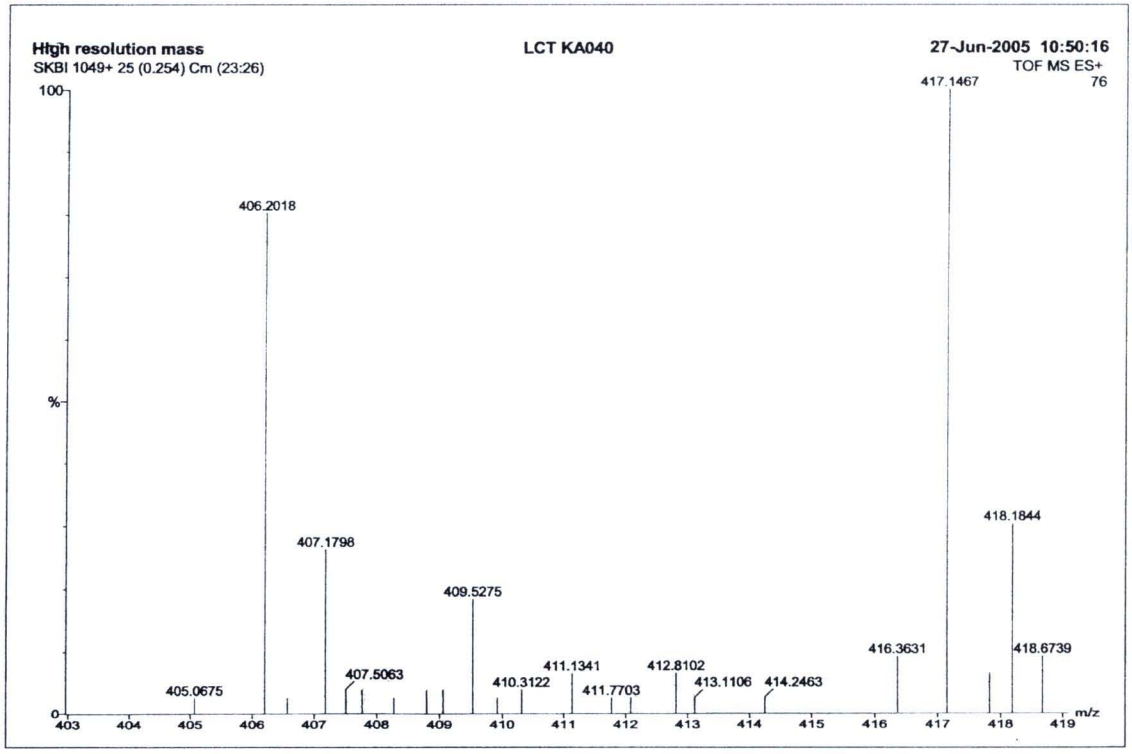

Figure 95 Mass spectrum of chaetoviridin F (**2.5**).

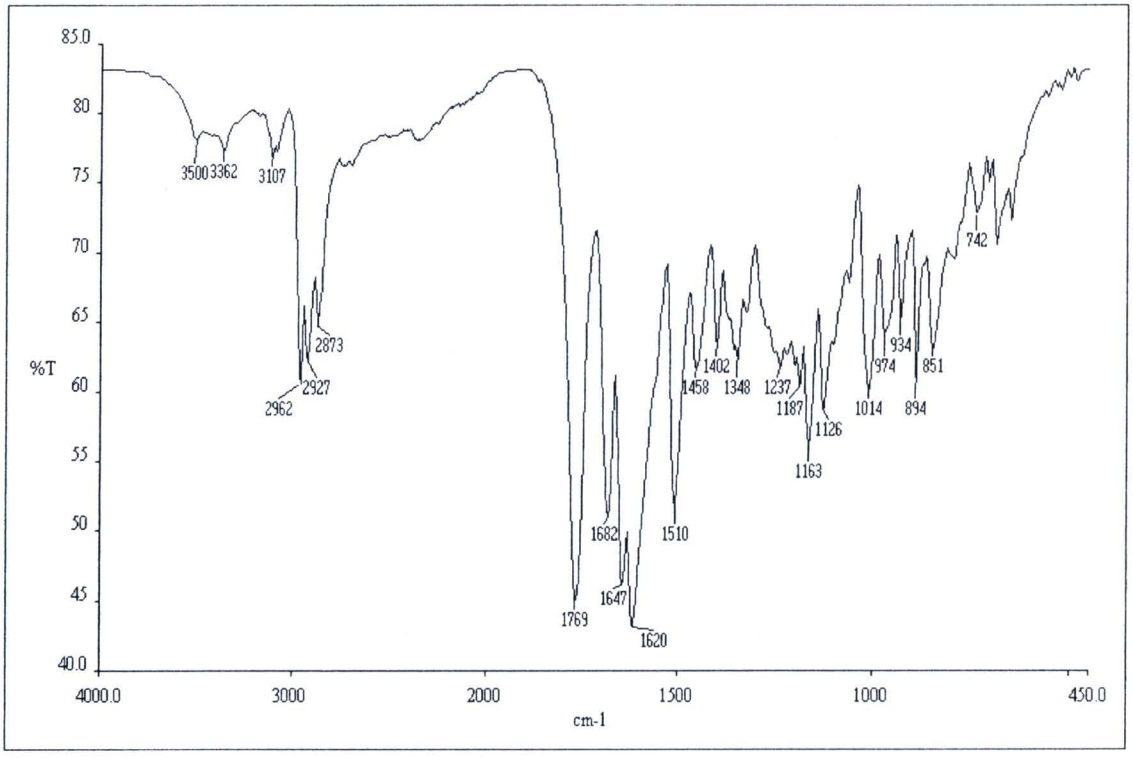

Figure 96 IR spectrum of chaetoviridin F (**2.5**).

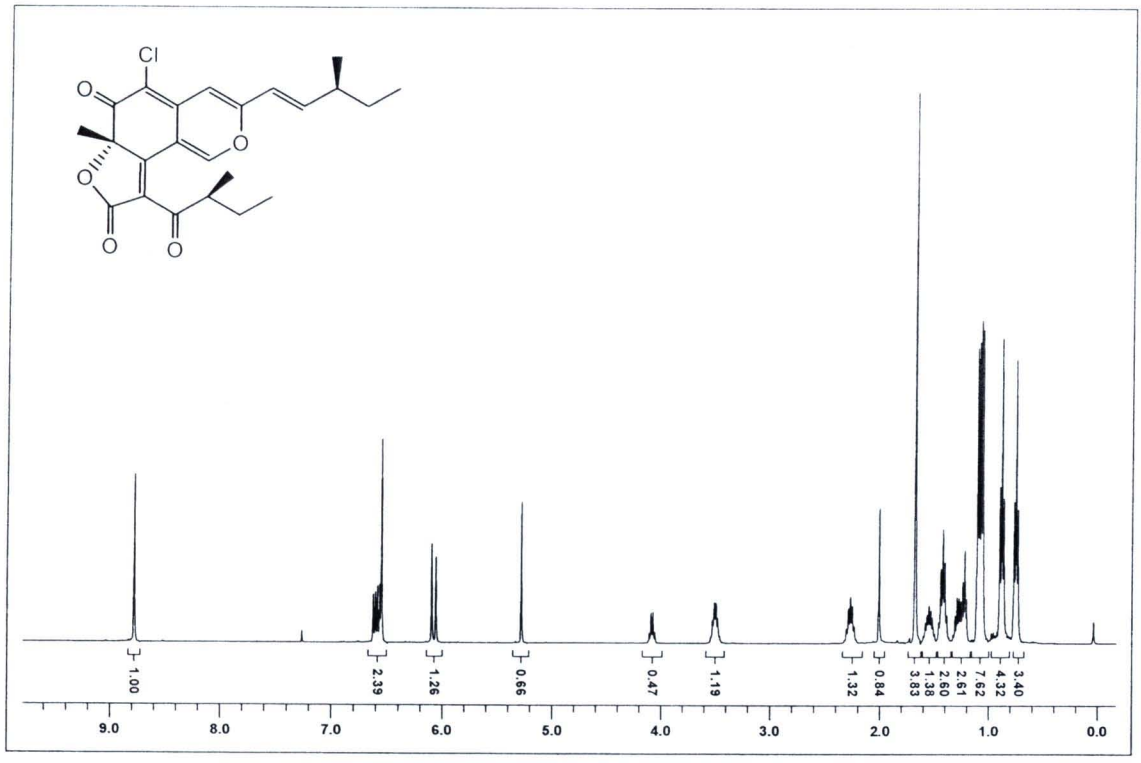

Figure 97 ^{1}H NMR spectrum of chaetoviridin F (**2.5**).

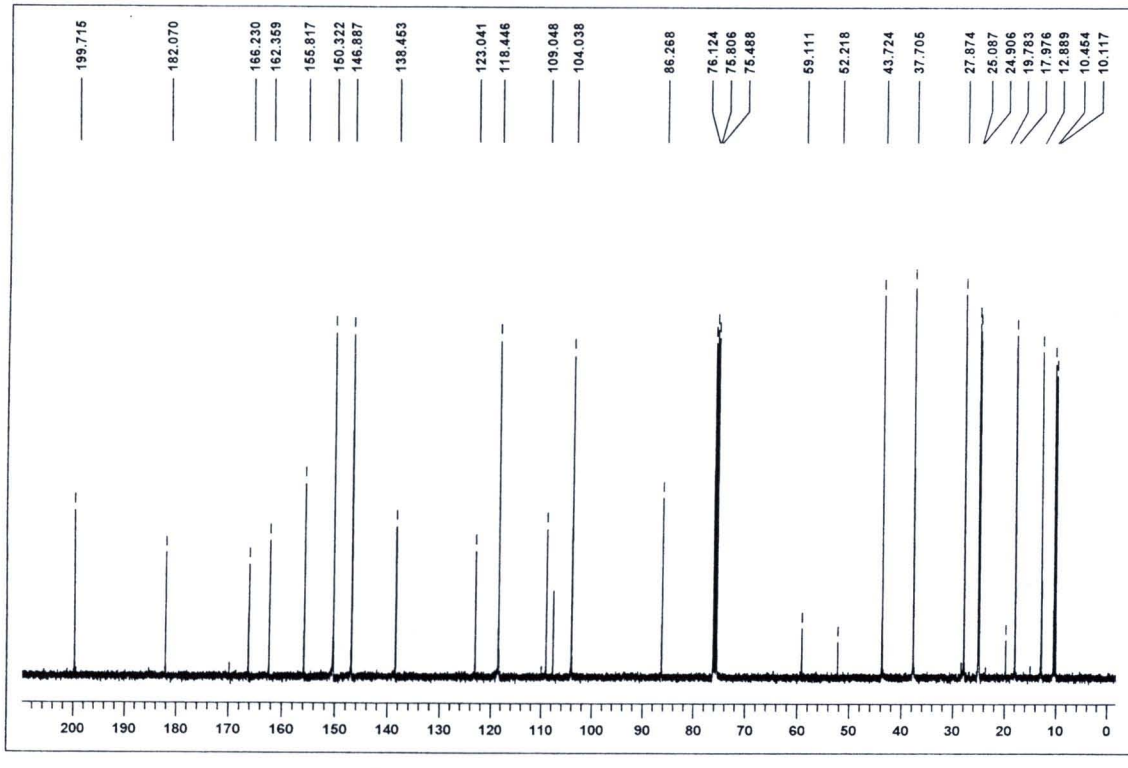

Figure 98 ^{13}C NMR spectrum of chaetoviridin F (**2.5**).

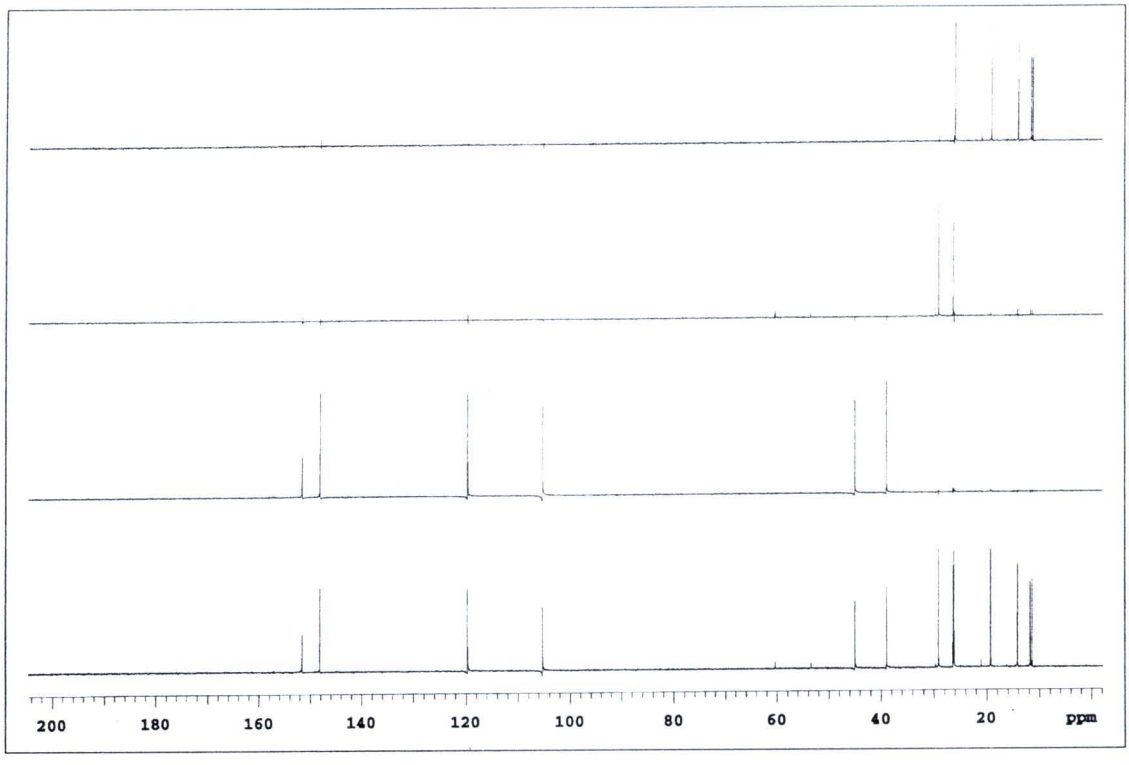

Figure 99 DEPT spectrum of chaetoviridin F (**2.5**).

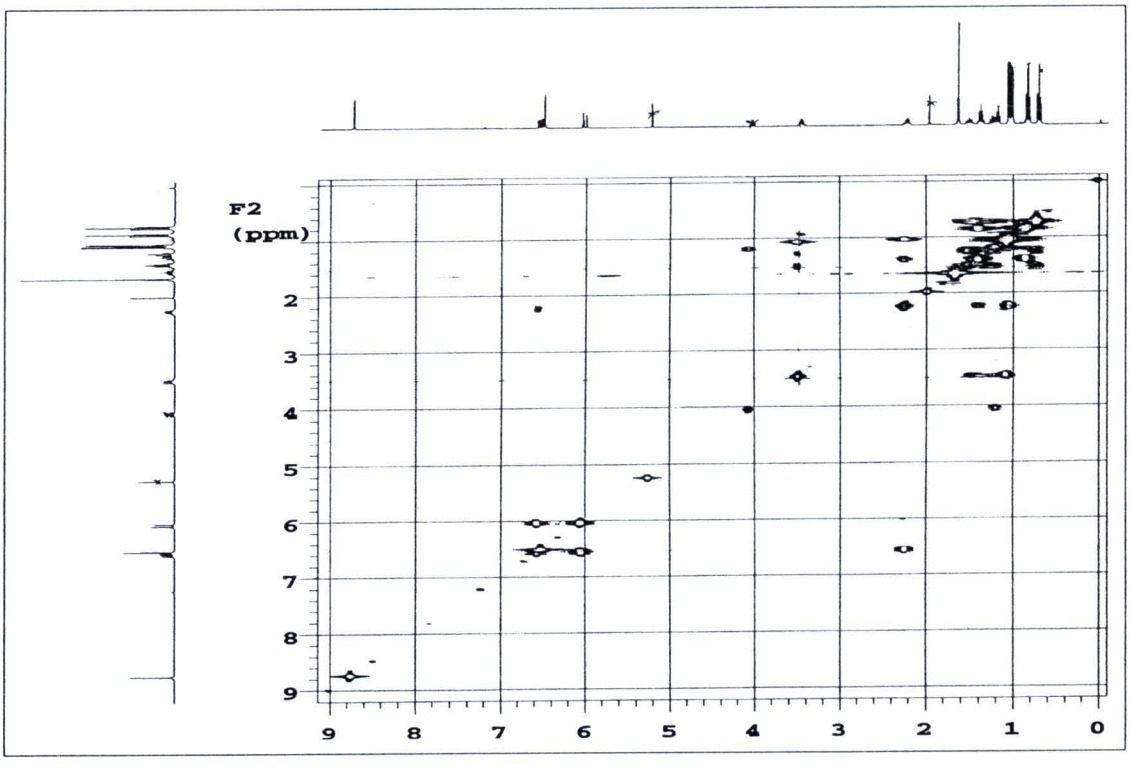

Figure 100 COSY spectrum of chaetoviridin F (**2.5**).

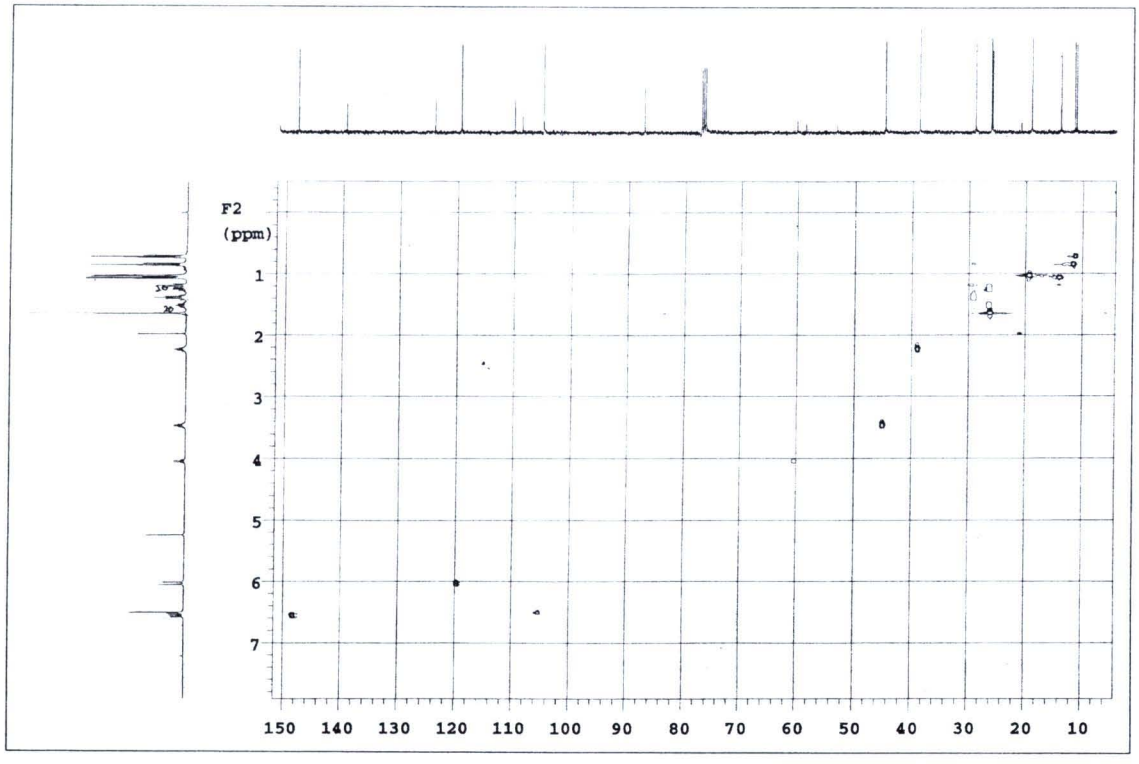

Figure 101 HSQC spectrum of chaetoviridin F (**2.5**).

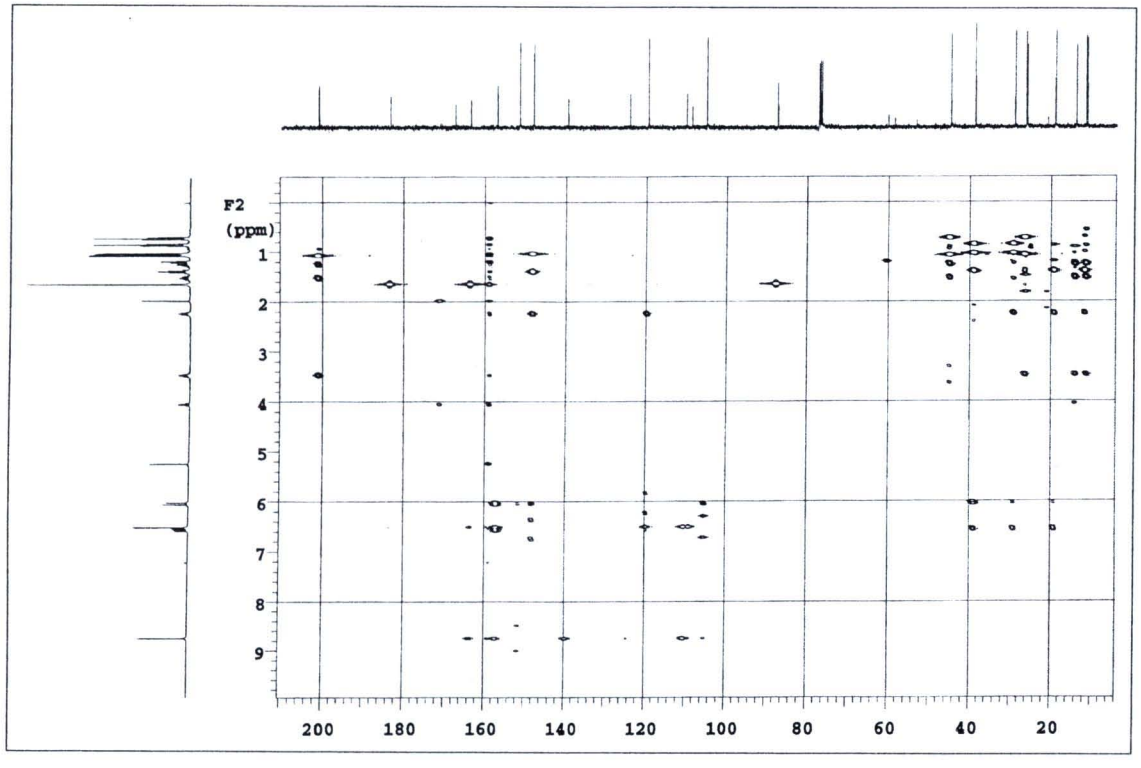

Figure 102 HMBC spectrum of chaetoviridin F (**2.5**).

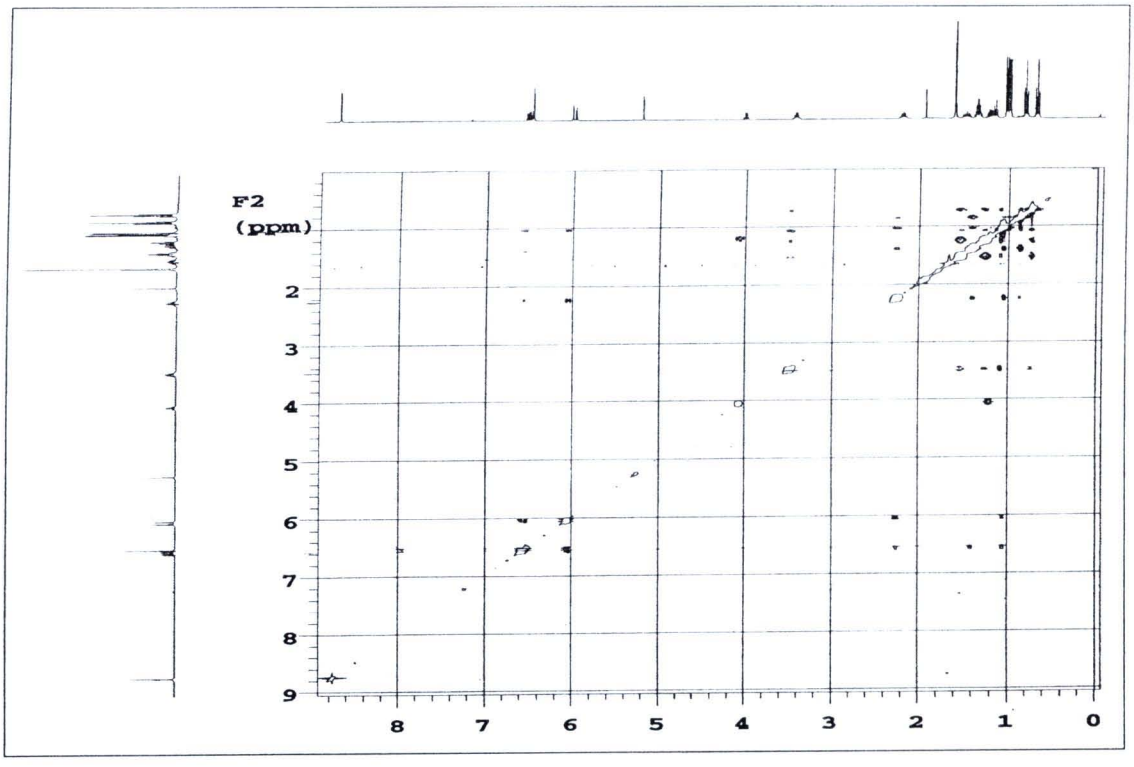

Figure 103 NOESY spectrum of chaetoviridin F (**2.5**).

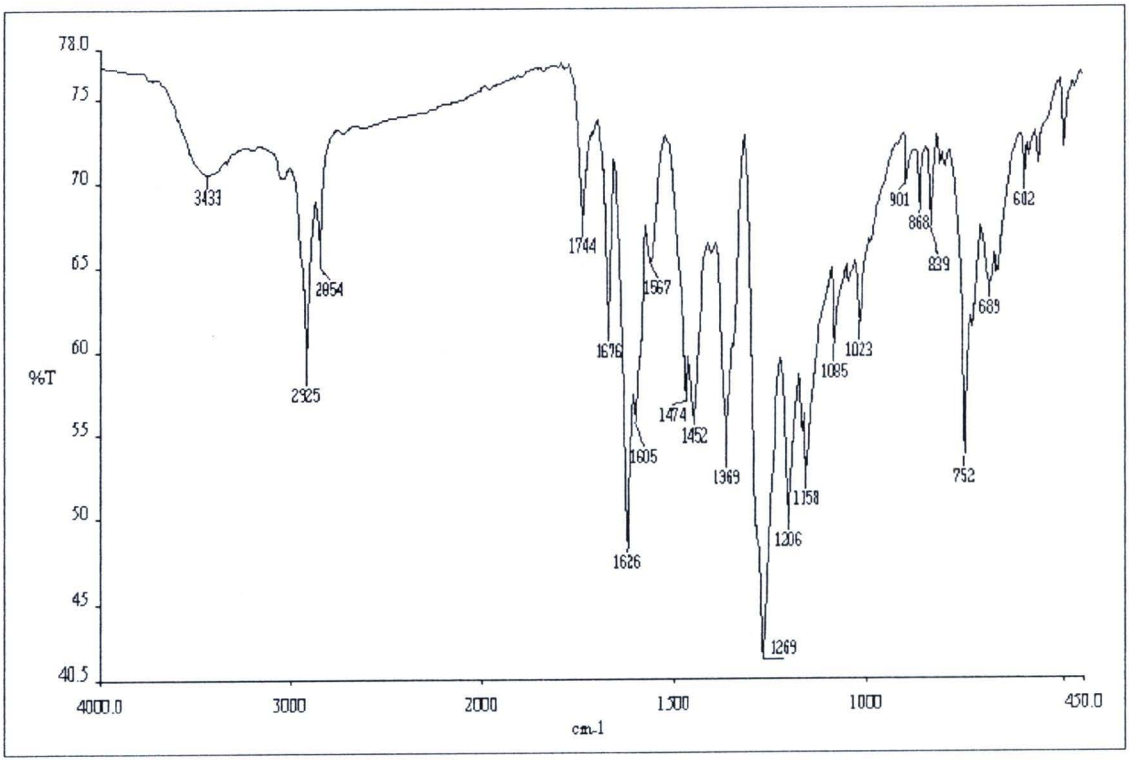

Figure 104 IR spectrum of chrysophanol (**2.6**).

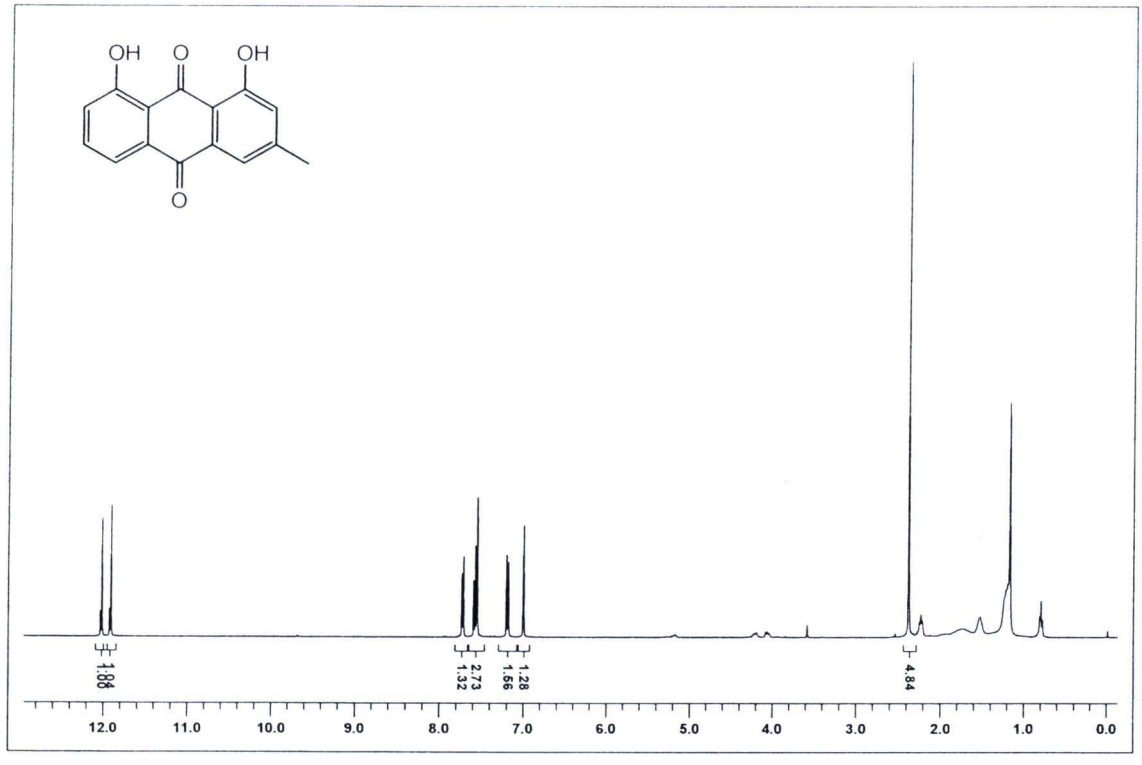

Figure 105 ^{1}H NMR spectrum of chrysophanol (**2.6**).

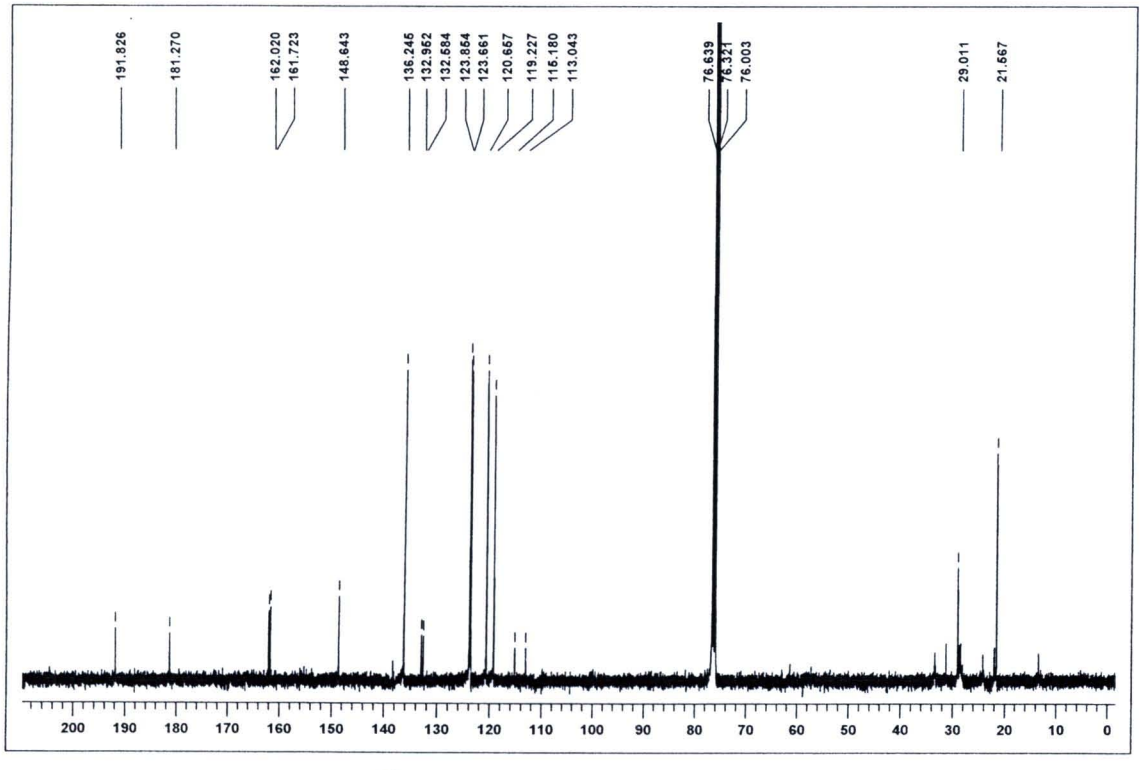

Figure 106 ^{13}C NMR spectrum of chrysophanol (**2.6**).

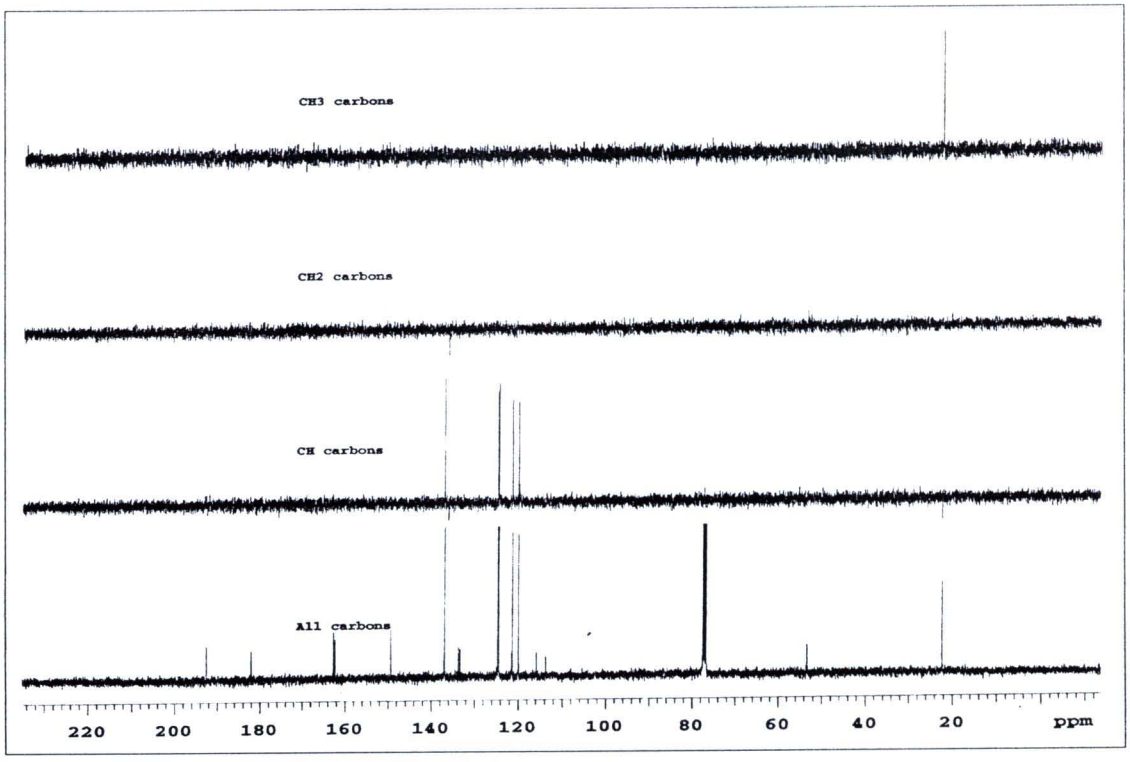

Figure 107 DEPT spectrum of chrysophanol (**2.6**).

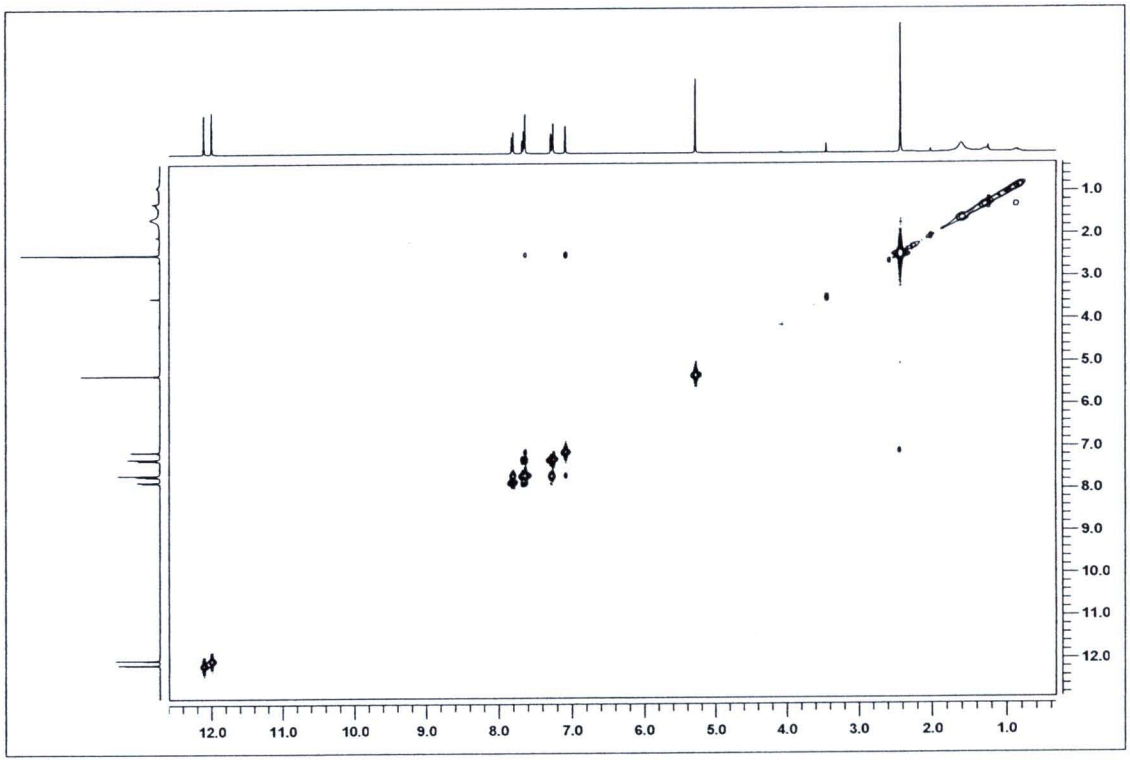

Figure 108 COSY spectrum of chrysophanol (**2.6**).

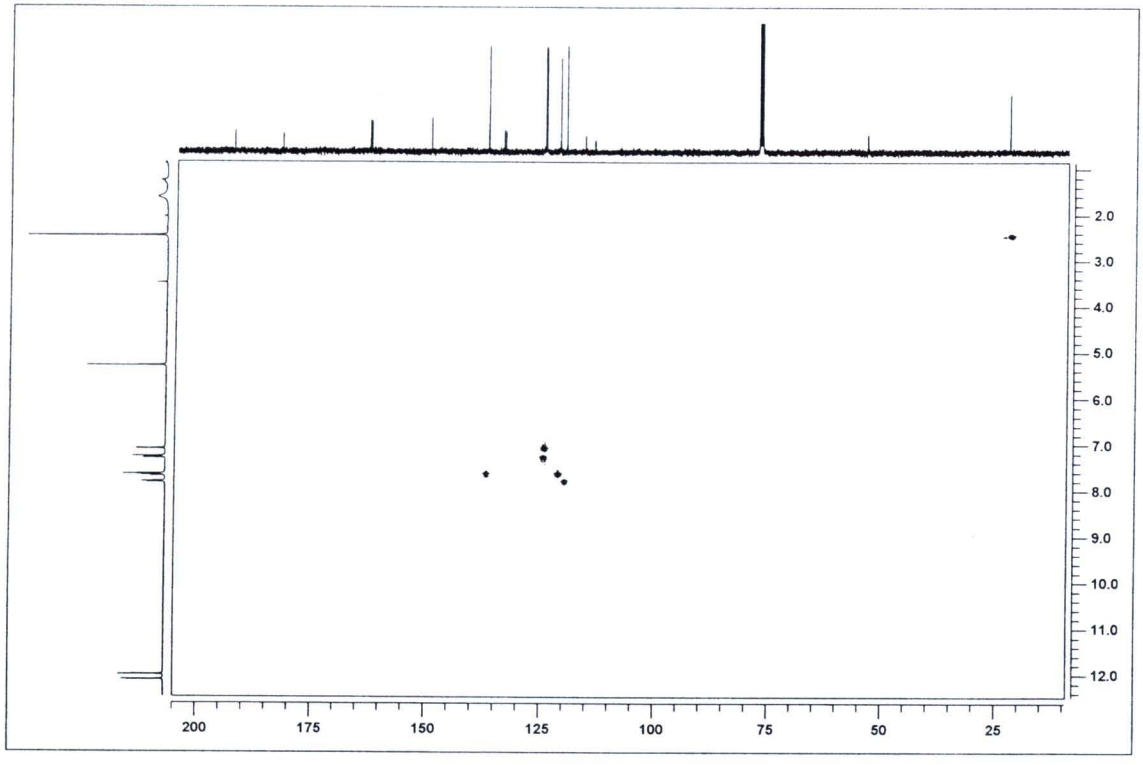

Figure 109 HSQC spectrum of chrysophanol (**2.6**).

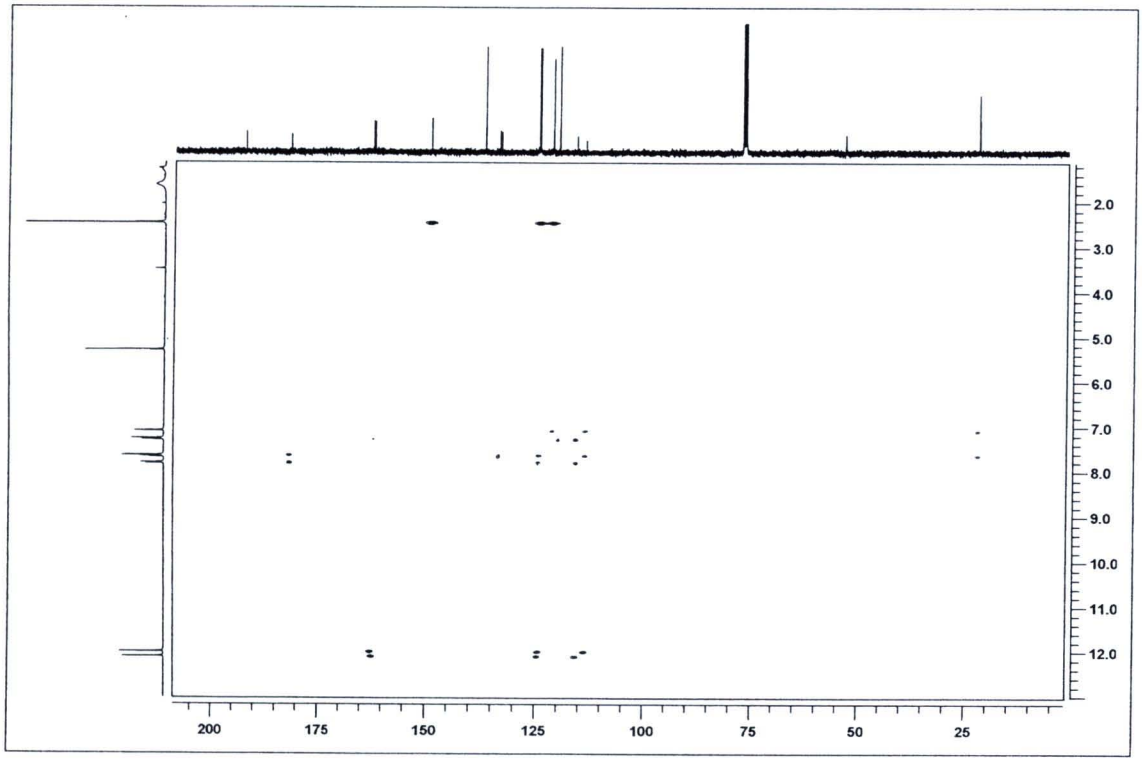

Figure 110 HMBC (CIGAR) spectrum of chrysophanol (**2.6**).

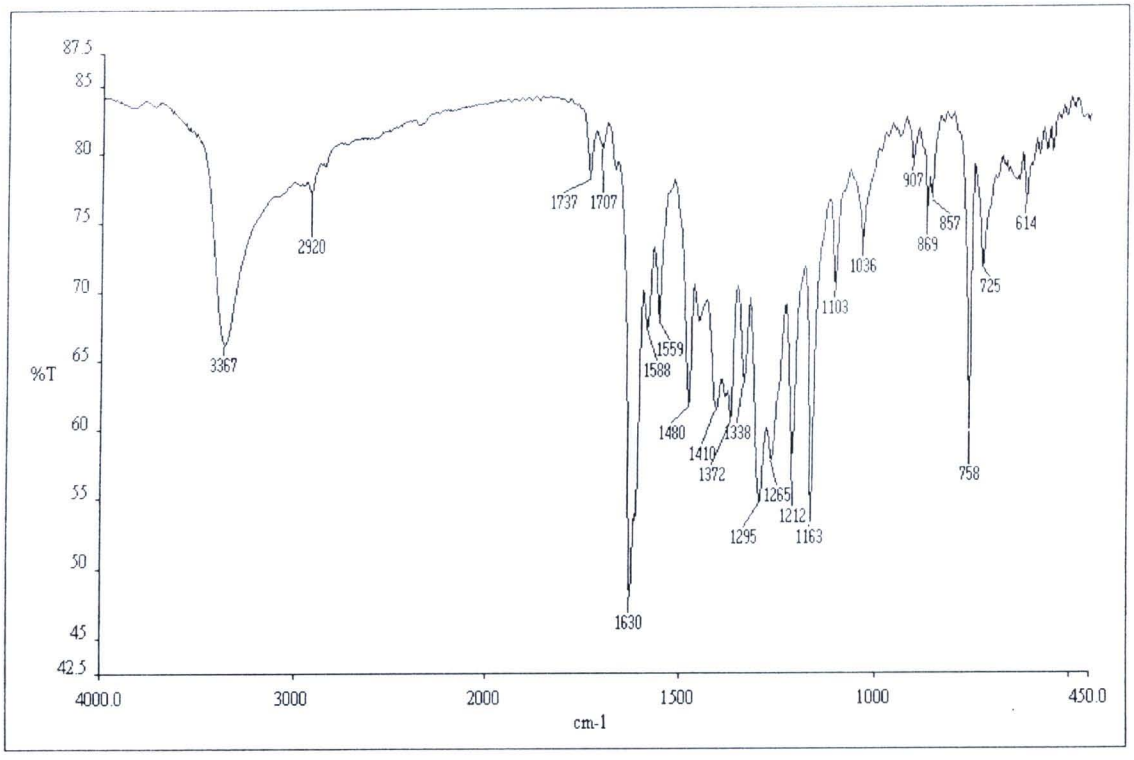

Figure 111 IR spectrum of emodin (**2.7**).

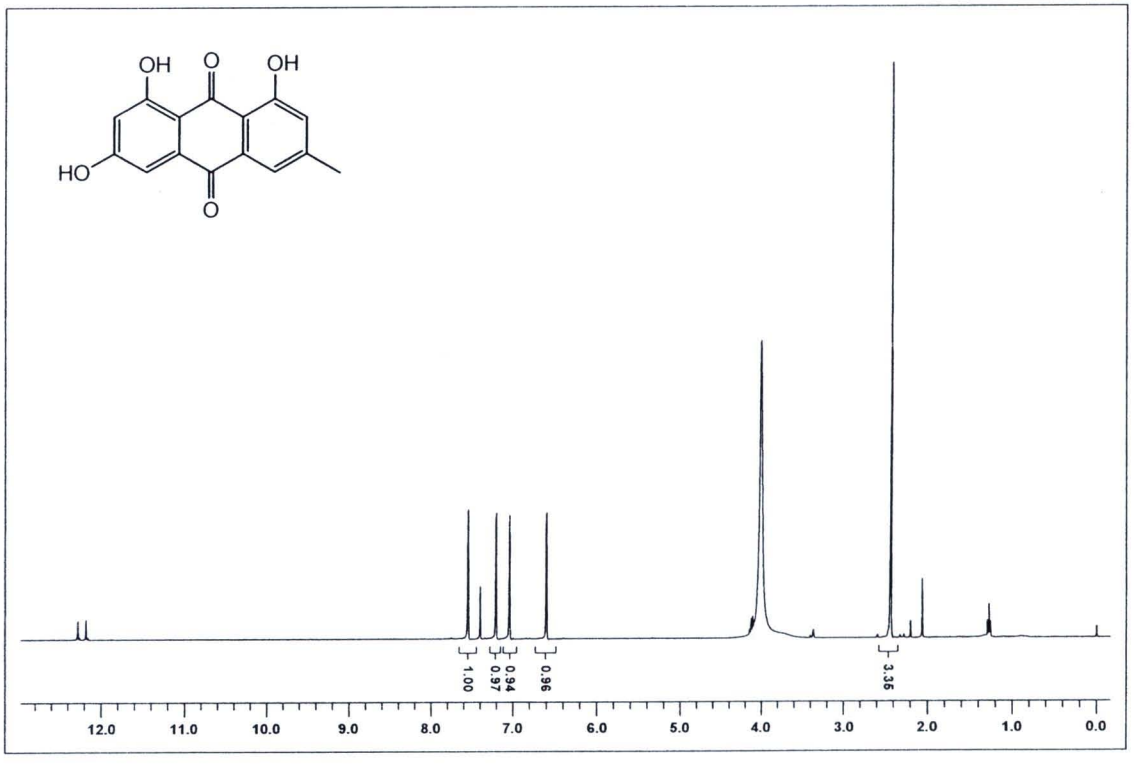

Figure 112 ^{1}H NMR spectrum of emodin (**2.7**).

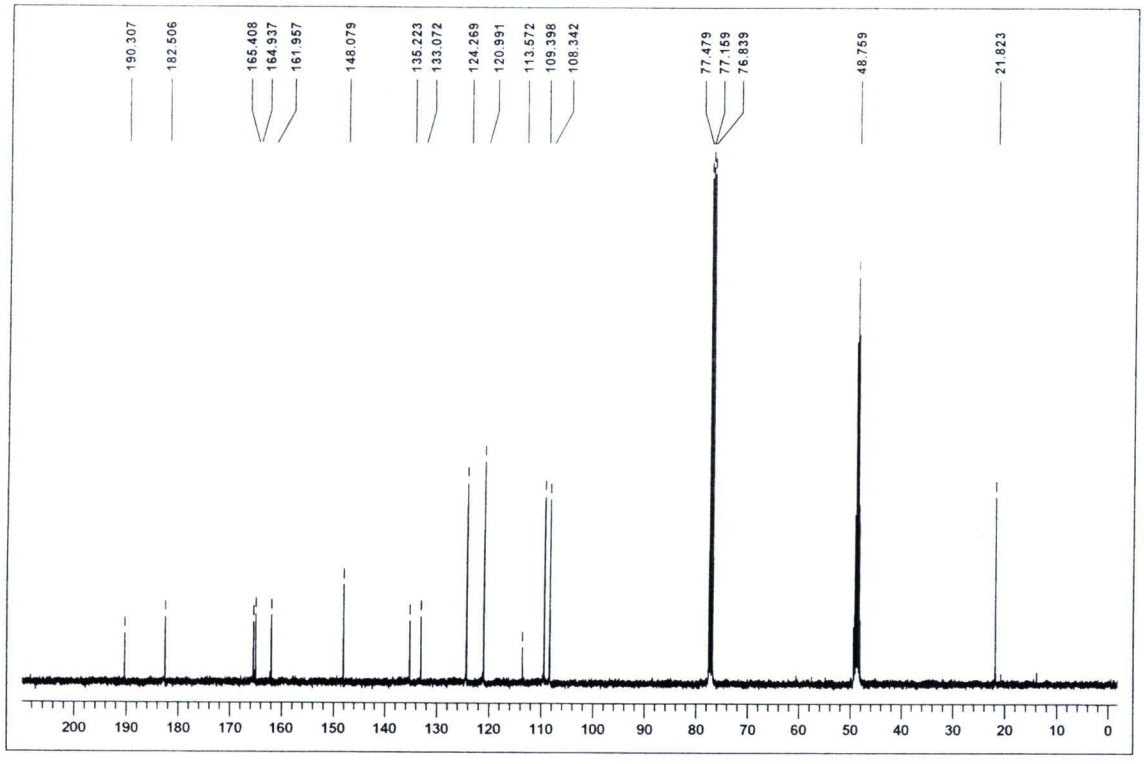

Figure 113 ^{13}C NMR spectrum of emodin (**2.7**).

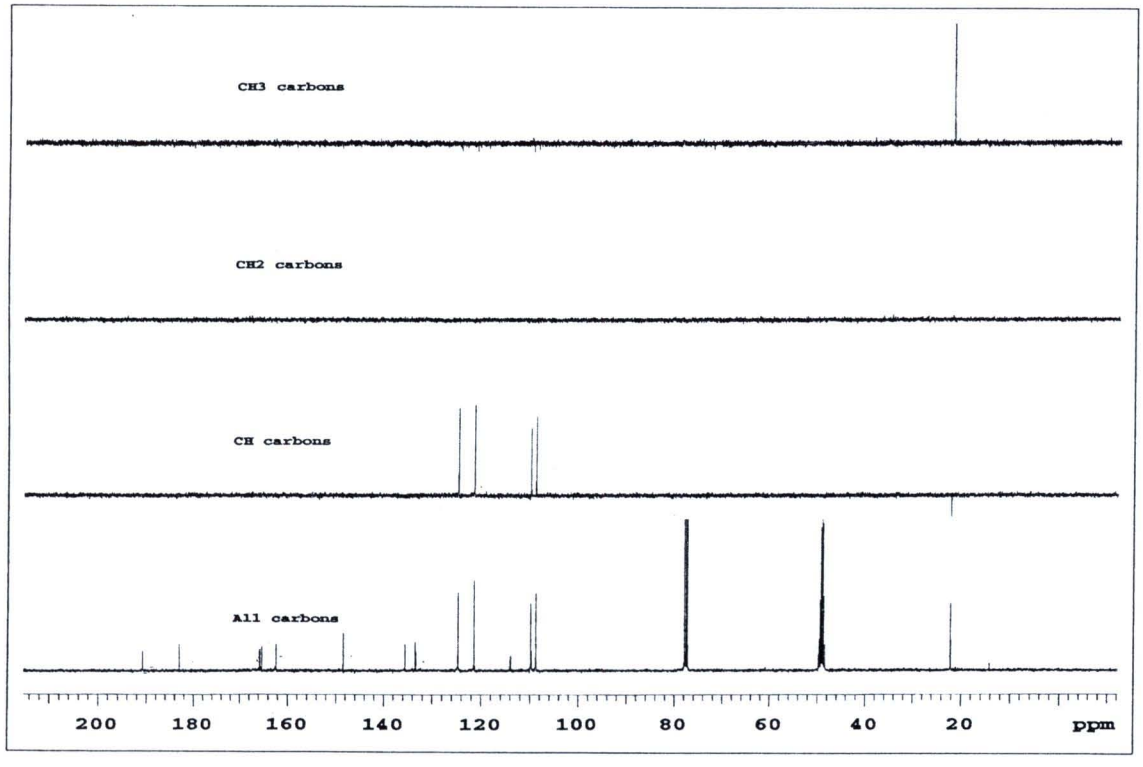

Figure 114 DEPT spectrum of emodin (**2.7**).

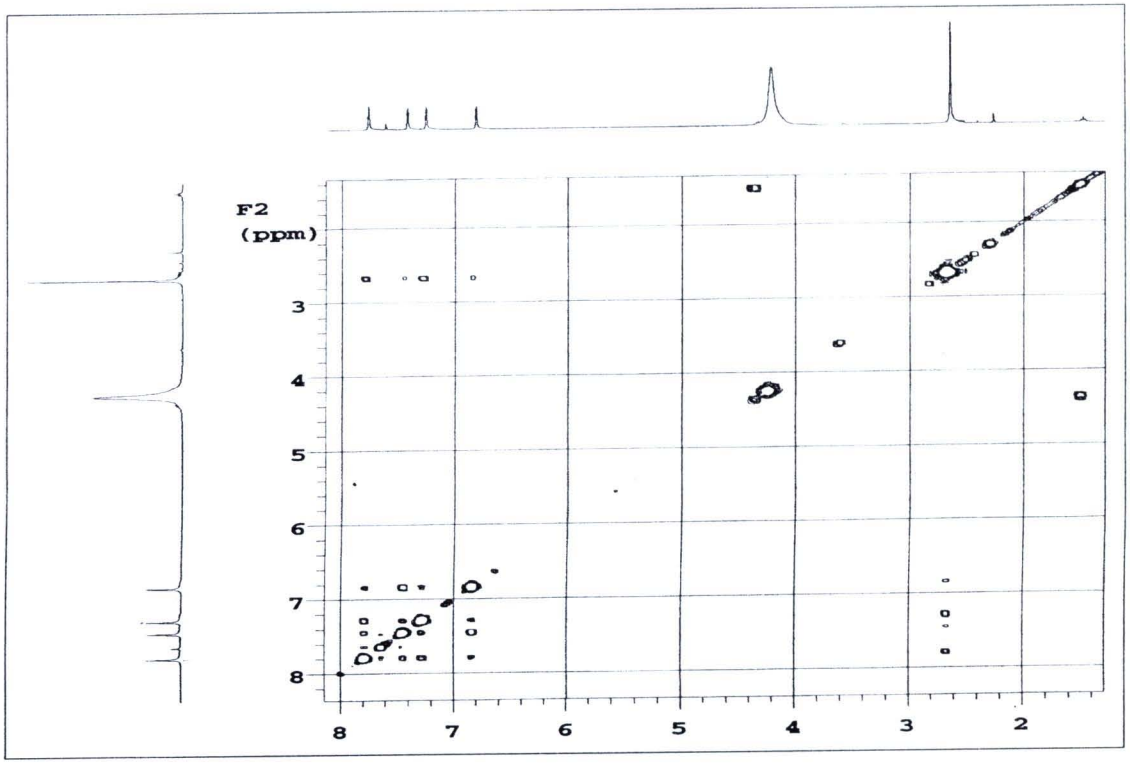

Figure 115 COSY spectrum of emodin (**2.7**).

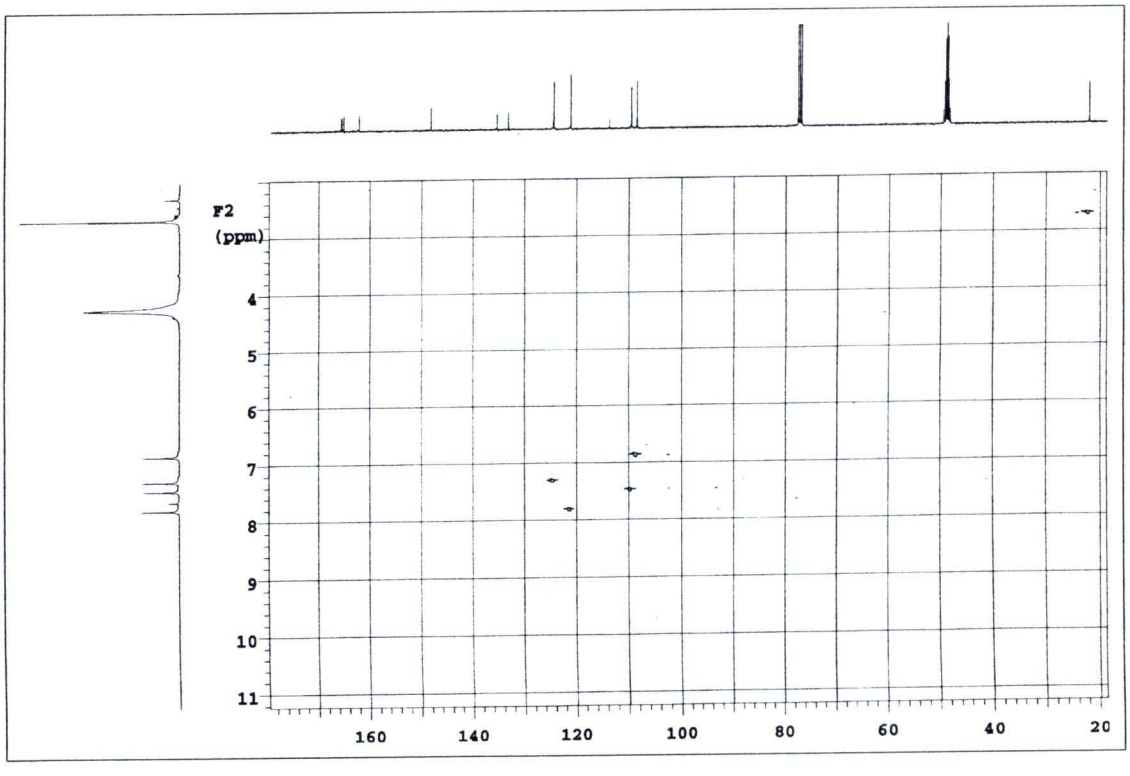

Figure 116 HMQC spectrum of emodin (**2.7**).

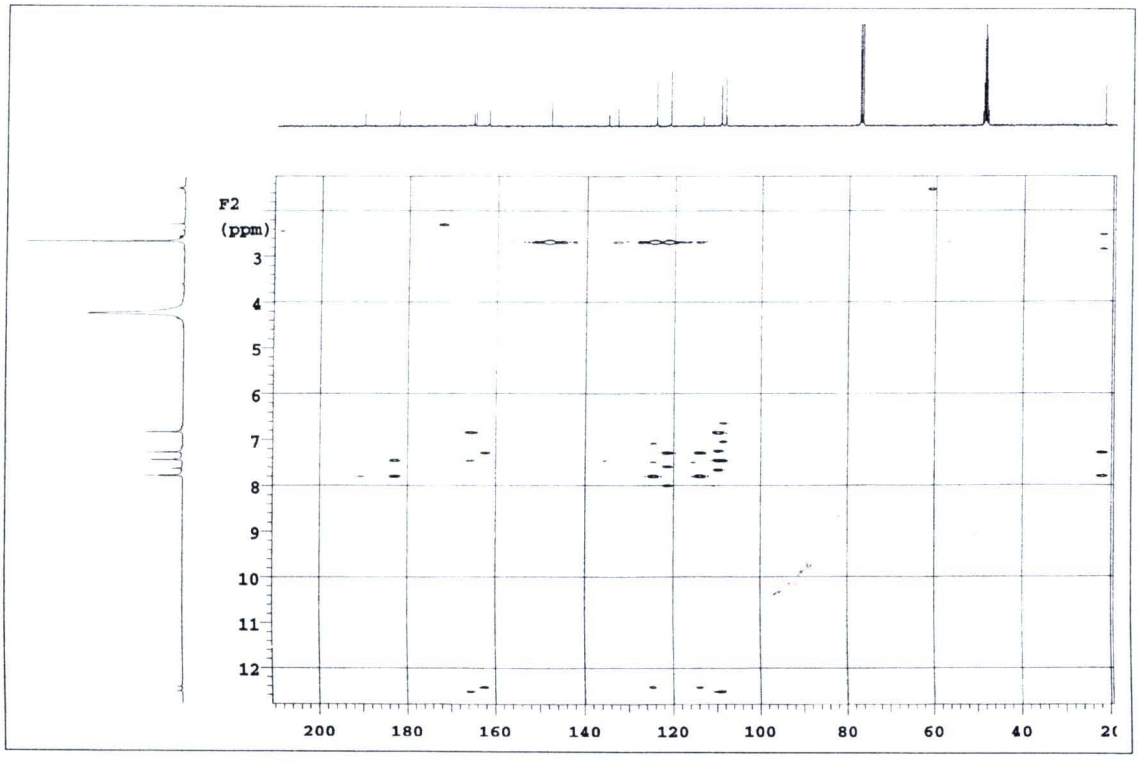

Figure 117 HMBC spectrum of emodin (**2.7**)

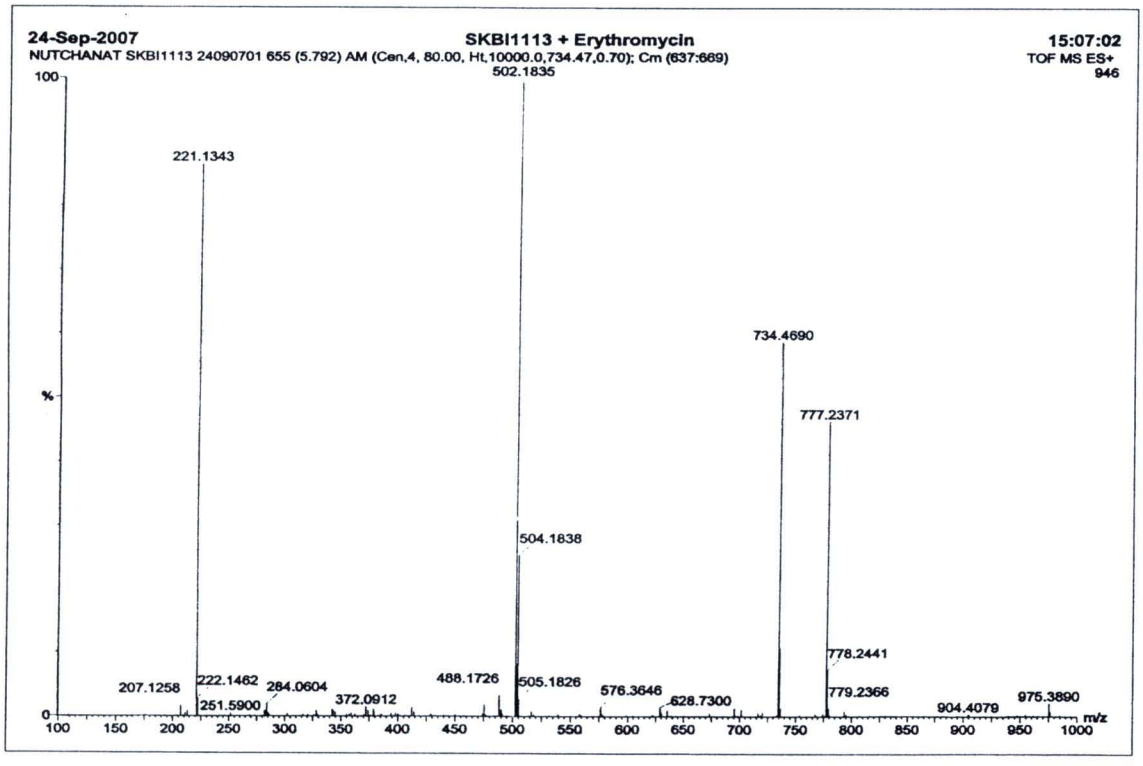

Figure 118 Mass spectrum of cochliodone D (**3.4**).

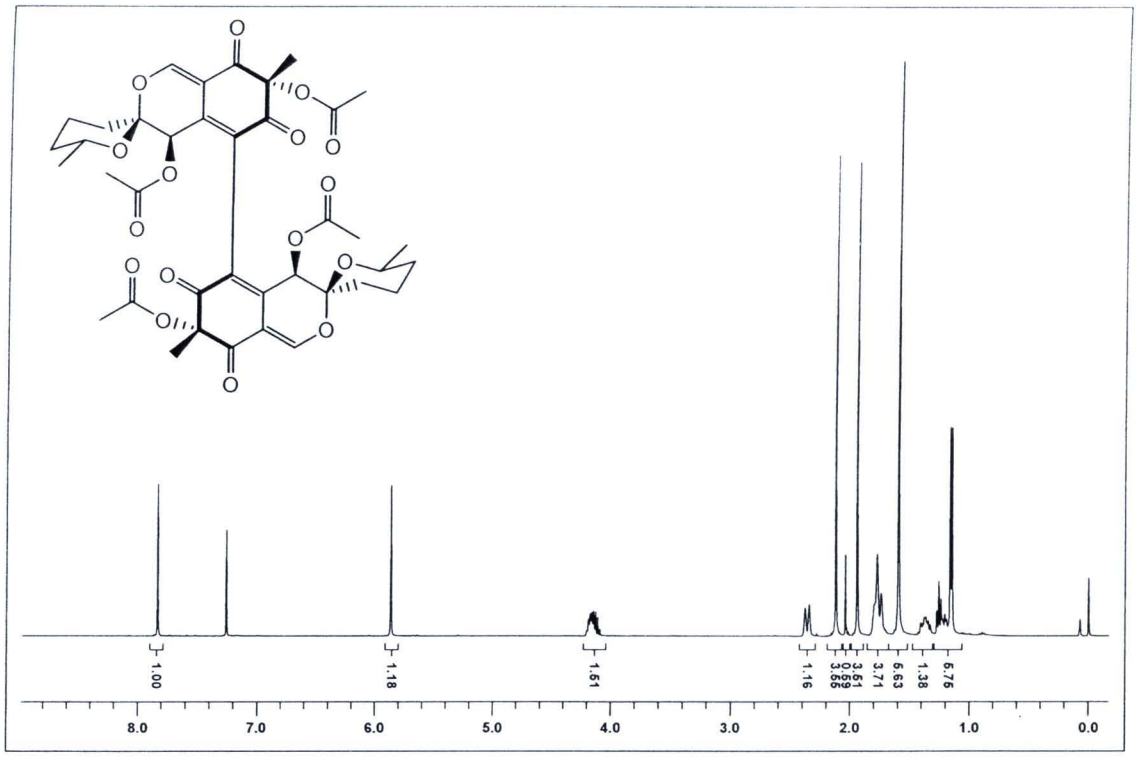

Figure 119 ^{1}H NMR spectrum of cochliodone D (**3.4**).

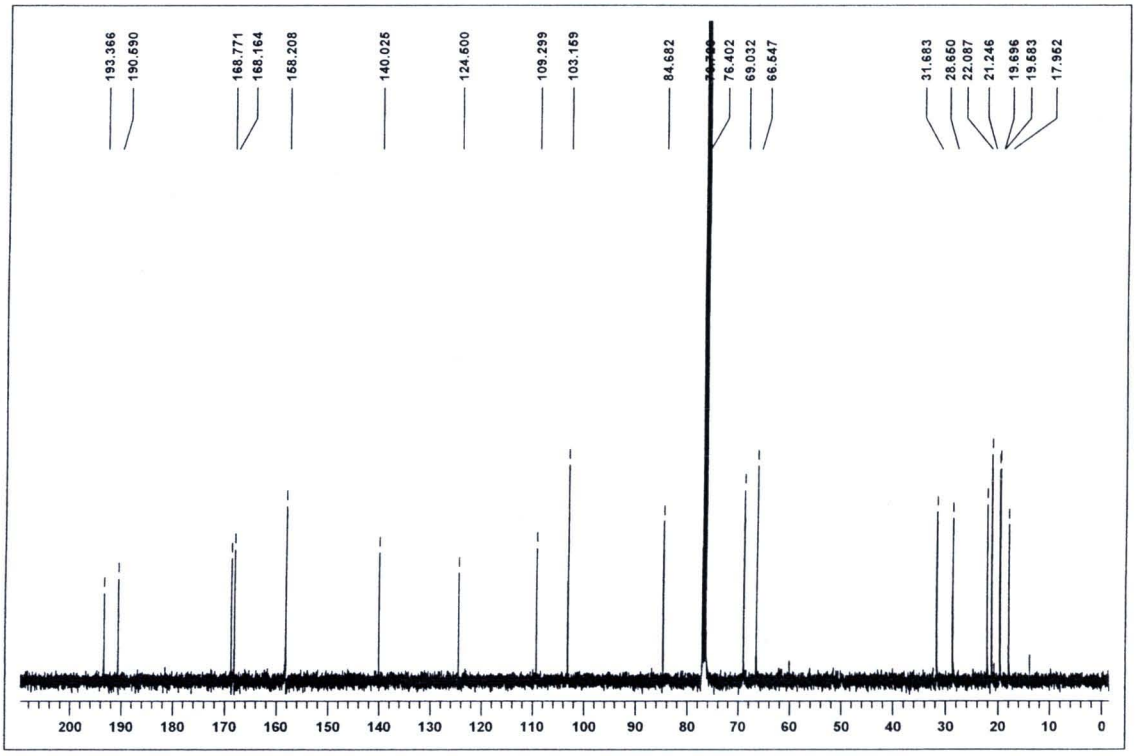

Figure 120 ^{13}C NMR spectrum of cochliodone D (**3.4**).

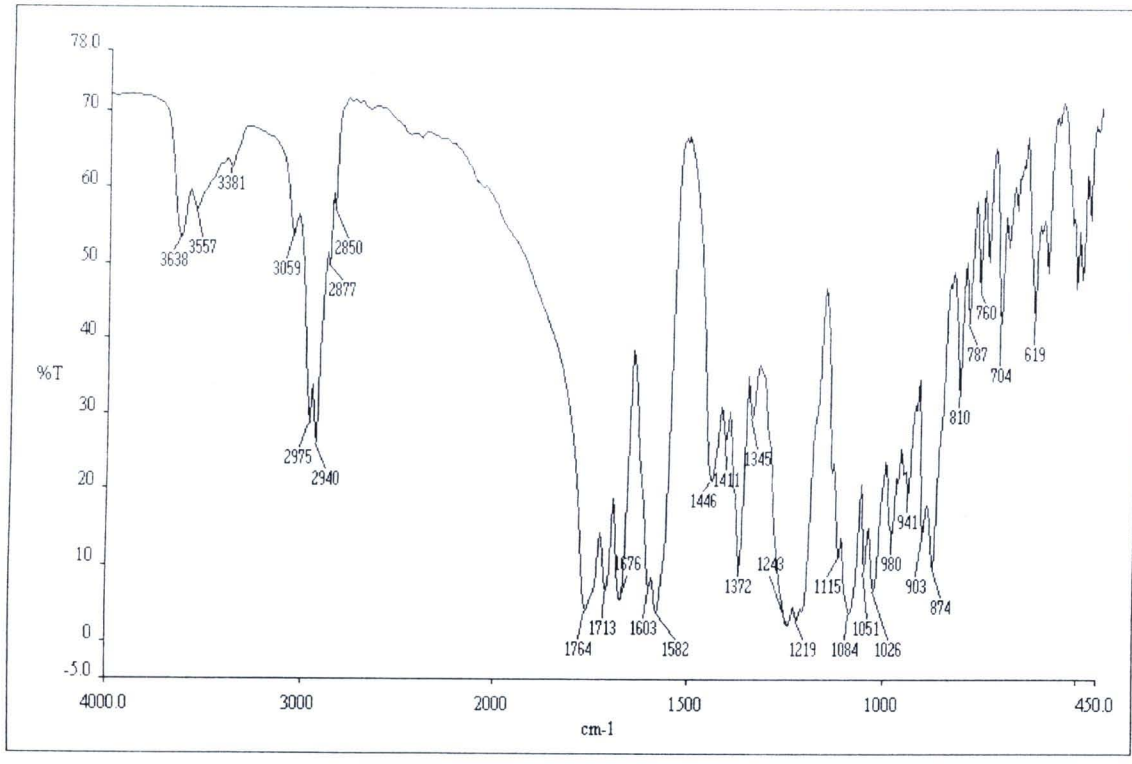

Figure 121 IR spectrum of cochliodone D (**3.4**).

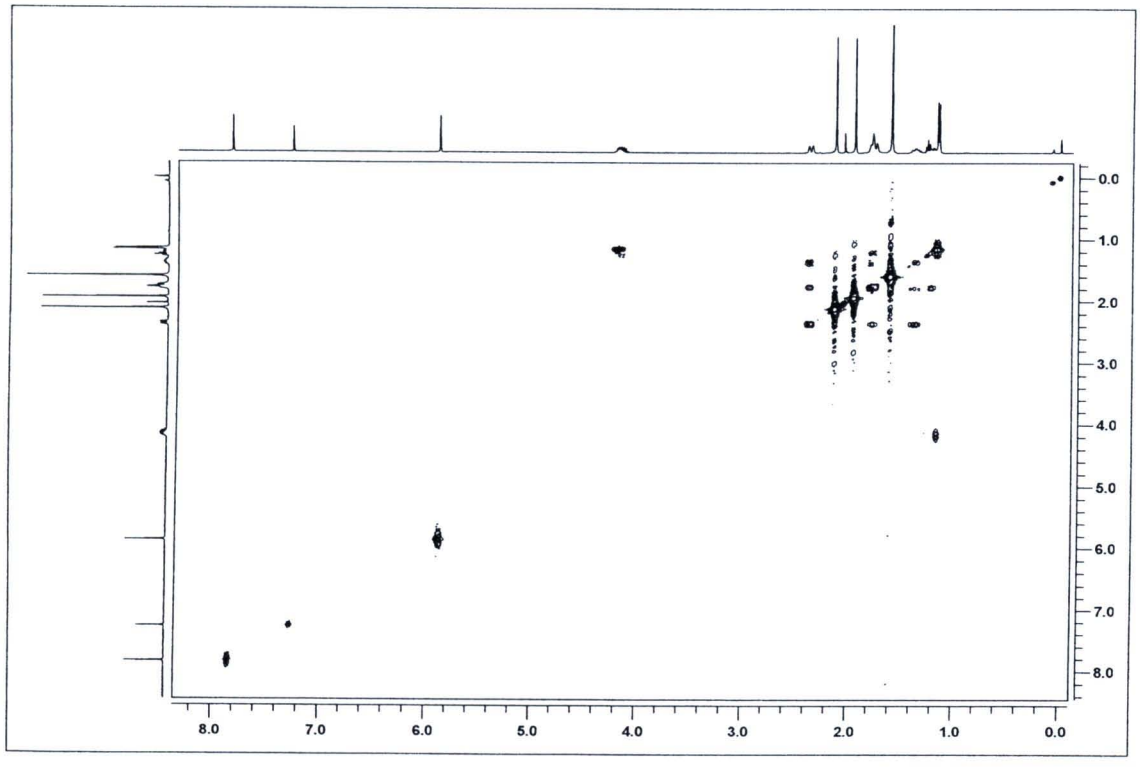

Figure 122 COSY spectrum of cochliodone D (**3.4**).

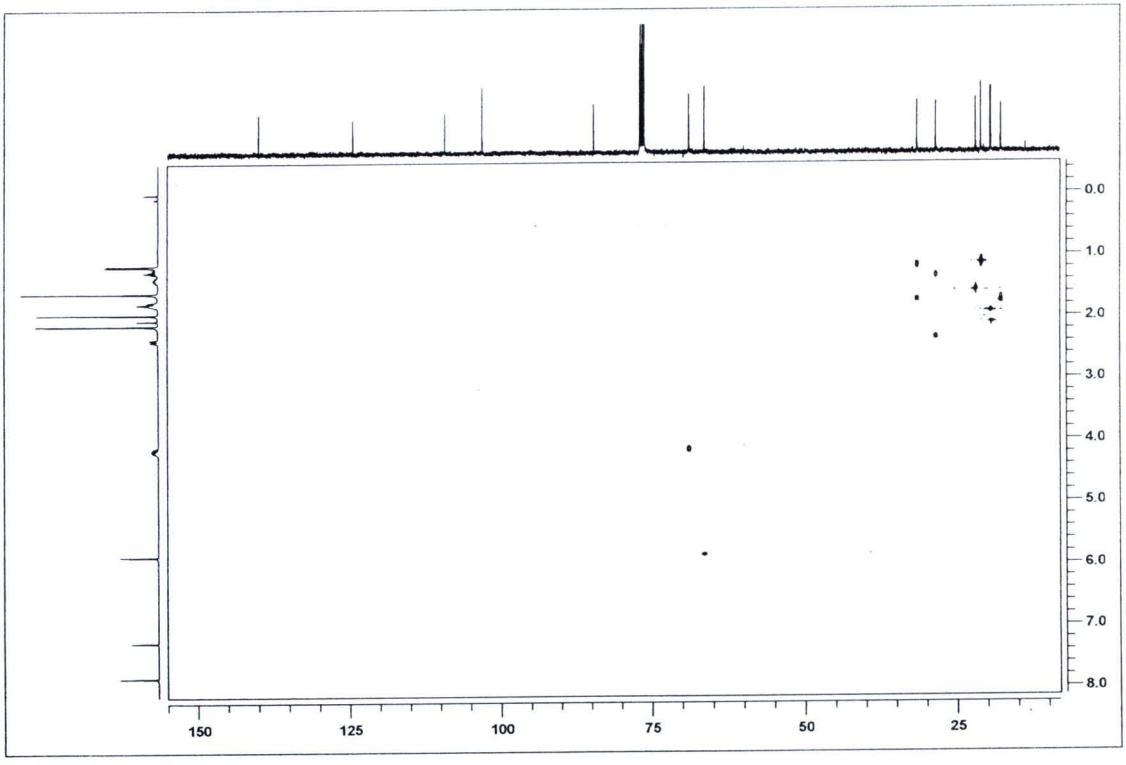

Figure 123 HSQC spectrum of cochliodone D **(3.4)**.

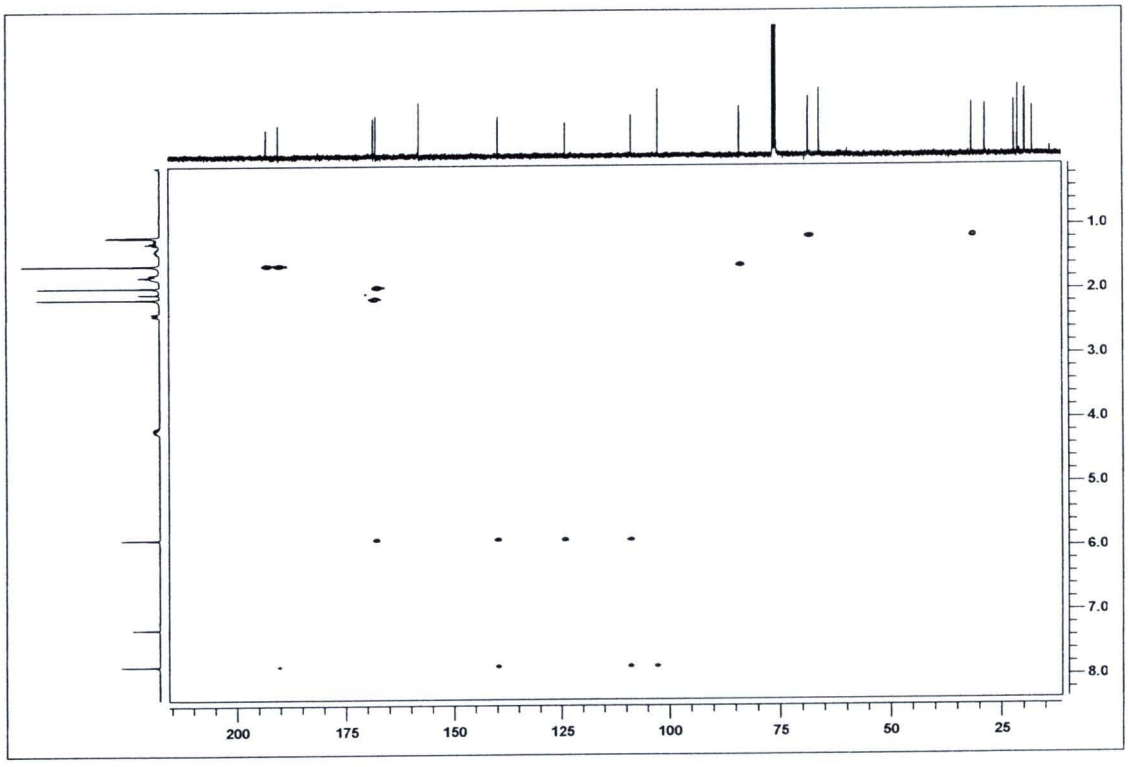

Figure 124 HMBC (CIGAR) spectrum of cochliodone D **(3.4)**.

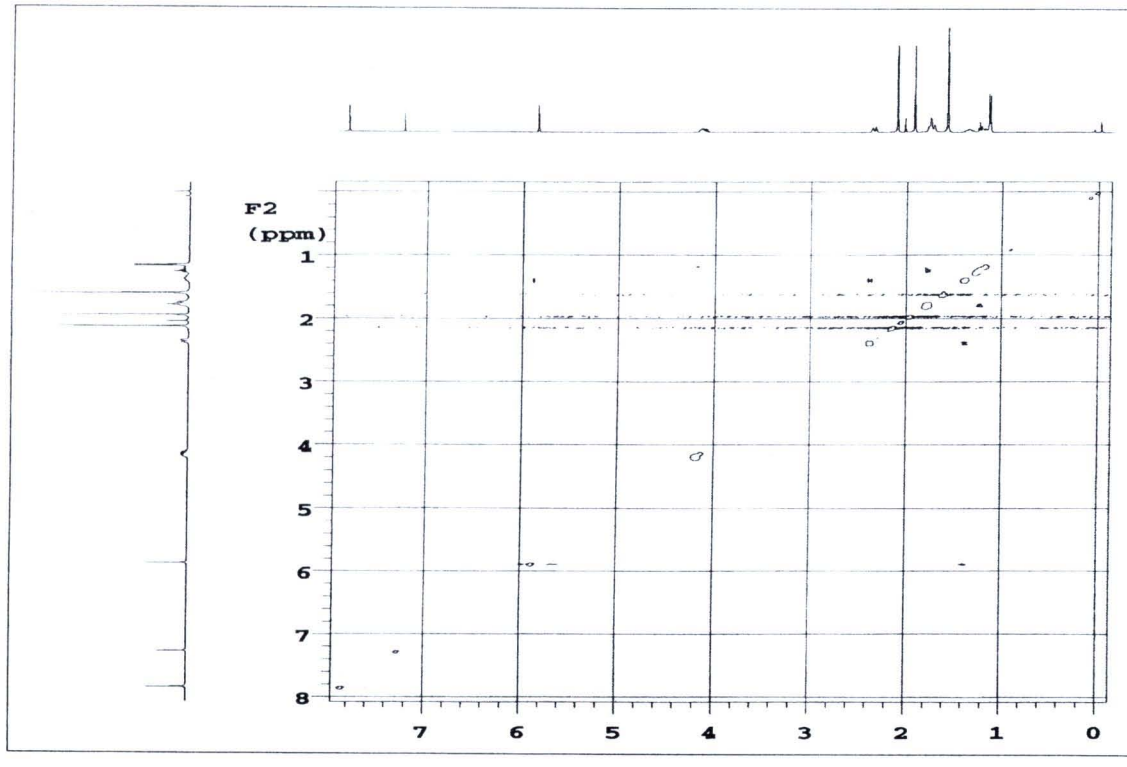

Figure 125 NOESY spectrum of cochliodone D (**3.4**).

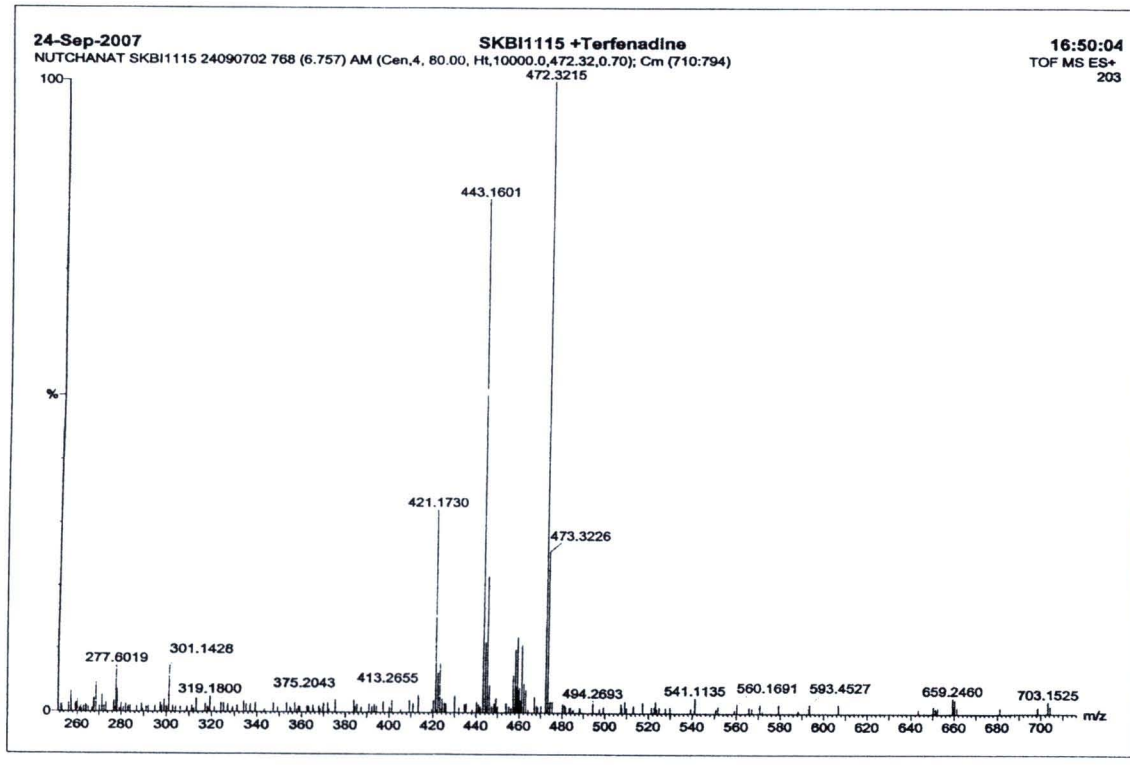

Figure 126 Mass spectrum of chaetoviridin G (**3.7**).

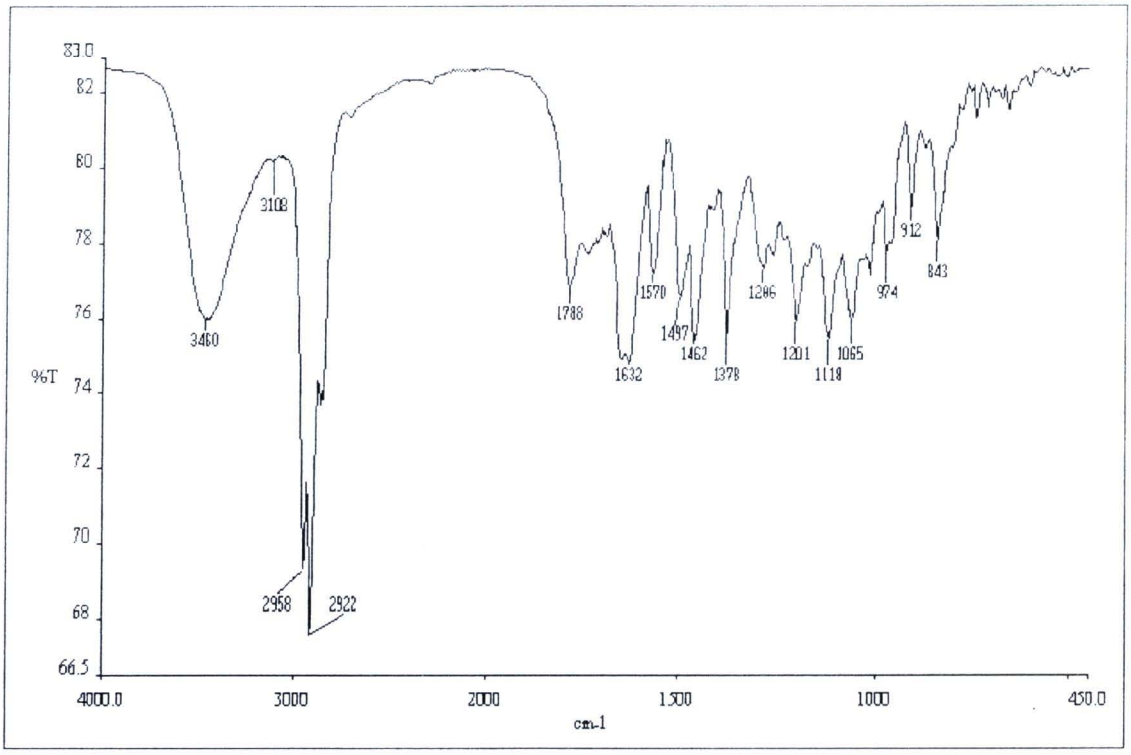

Figure 127 IR spectrum of chaetoviridin G (**3.7**).

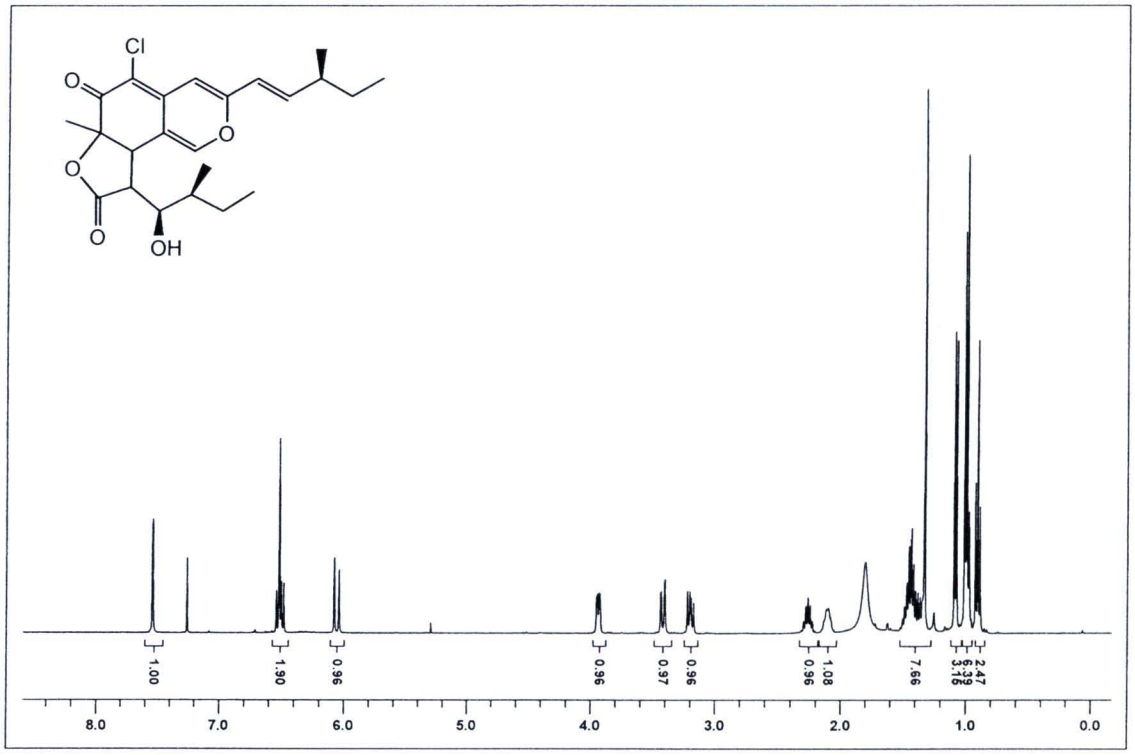

Figure 128 ^{1}H NMR spectrum of chaetoviridin G (**3.7**).

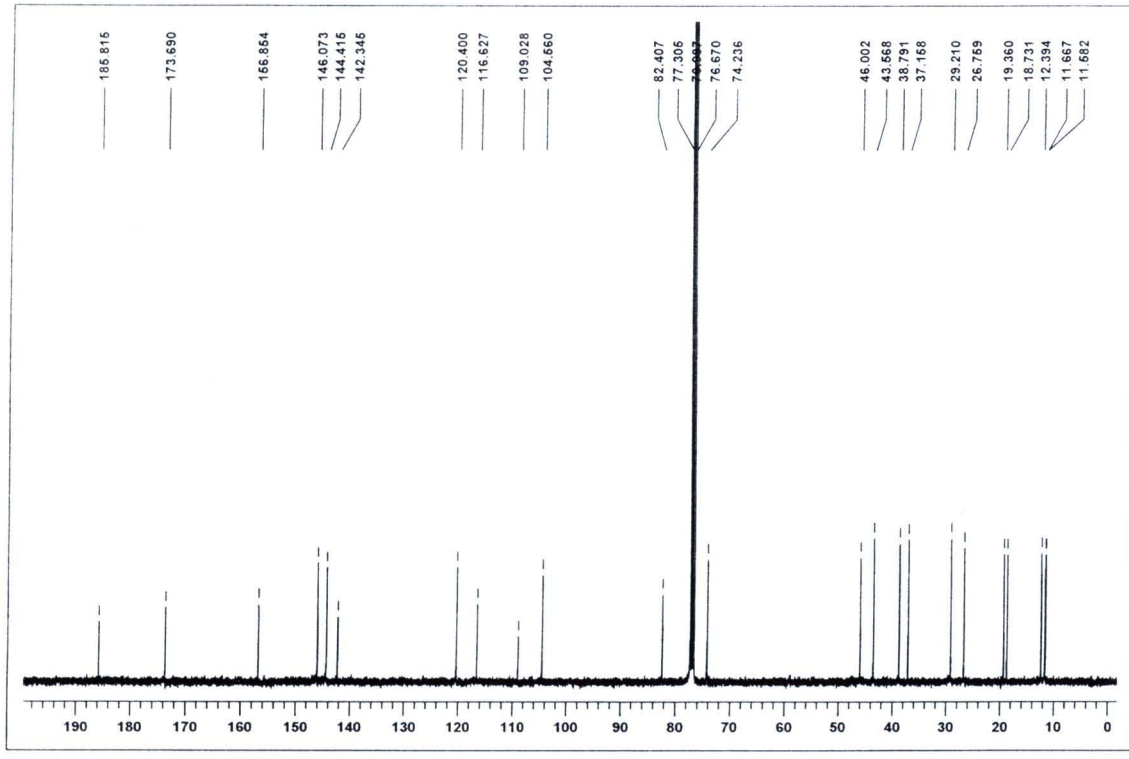

Figure 129 ^{13}C NMR spectrum of chaetoviridin G (**3.7**).

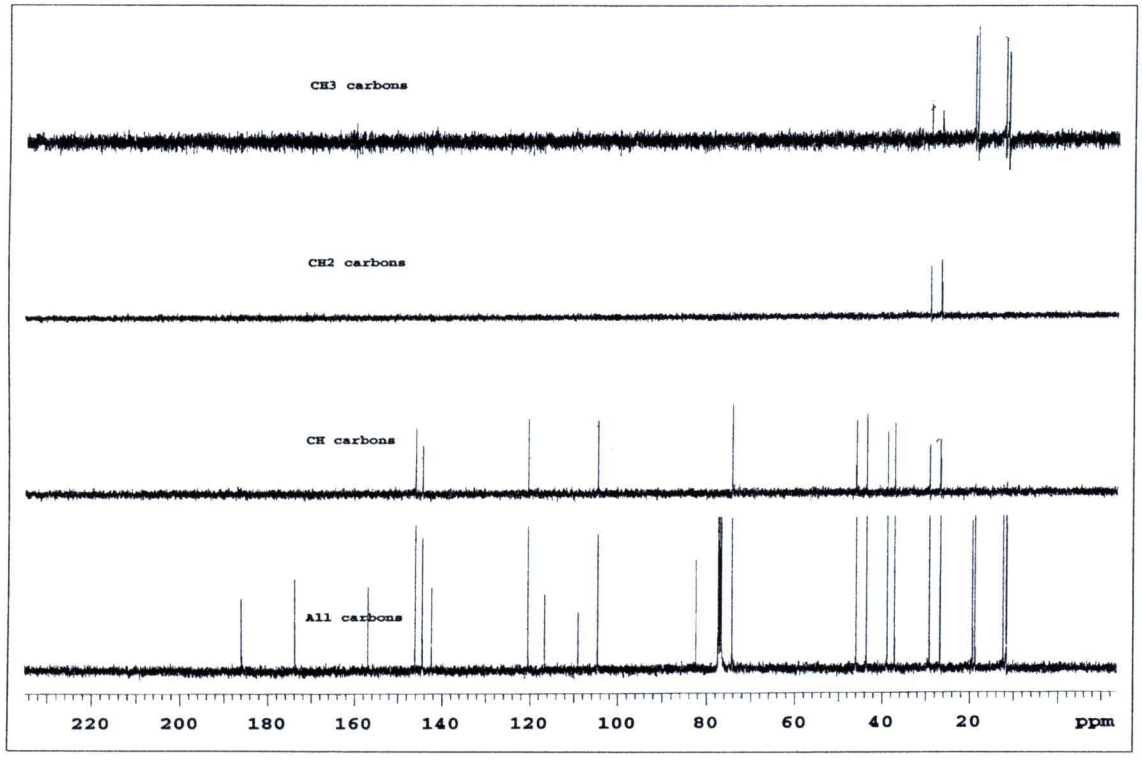

Figure 130 DEPT spectrum of chaetoviridin G 3.7).

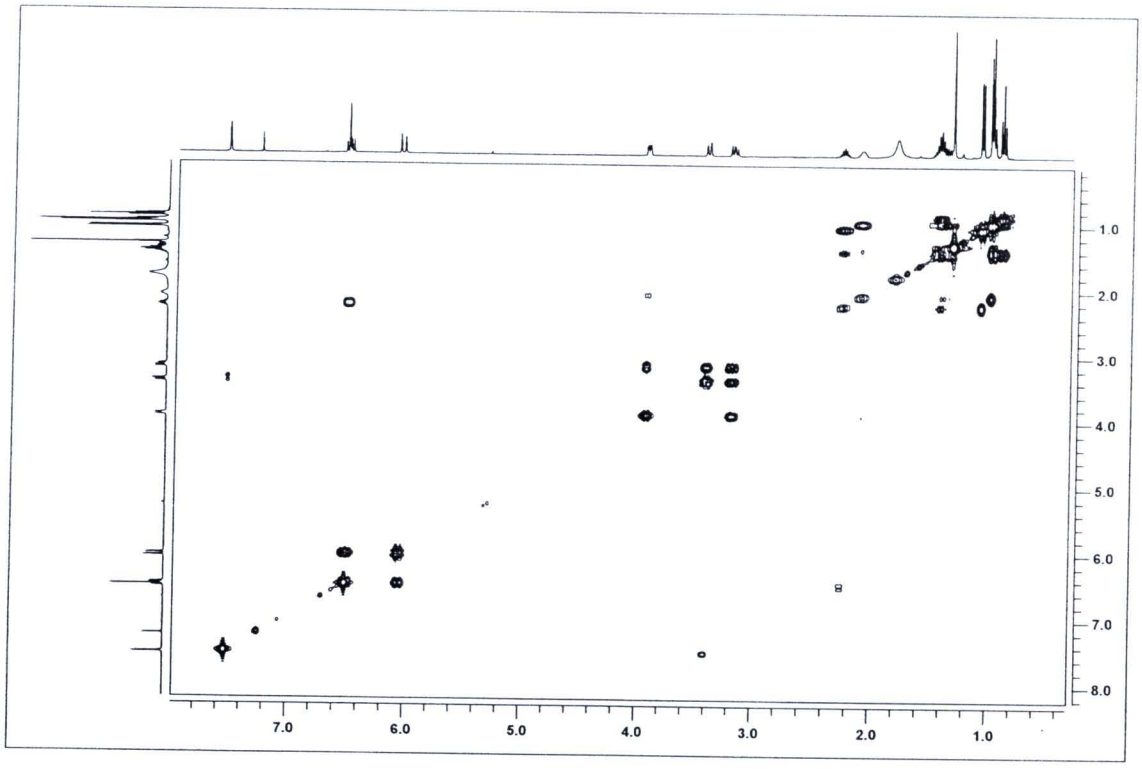

Figure 131 COSY spectrum of chaetoviridin G (**3.7**).

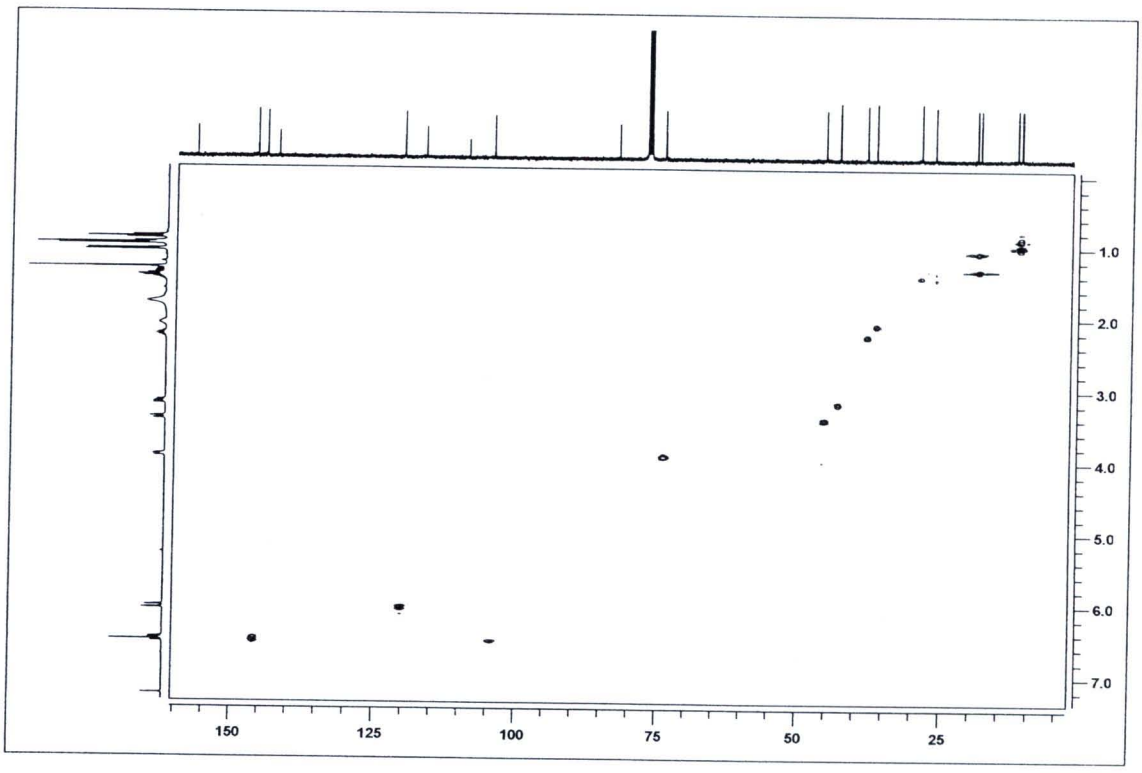

Figure 132 HSQC spectrum of chaetoviridin G (**3.7**).

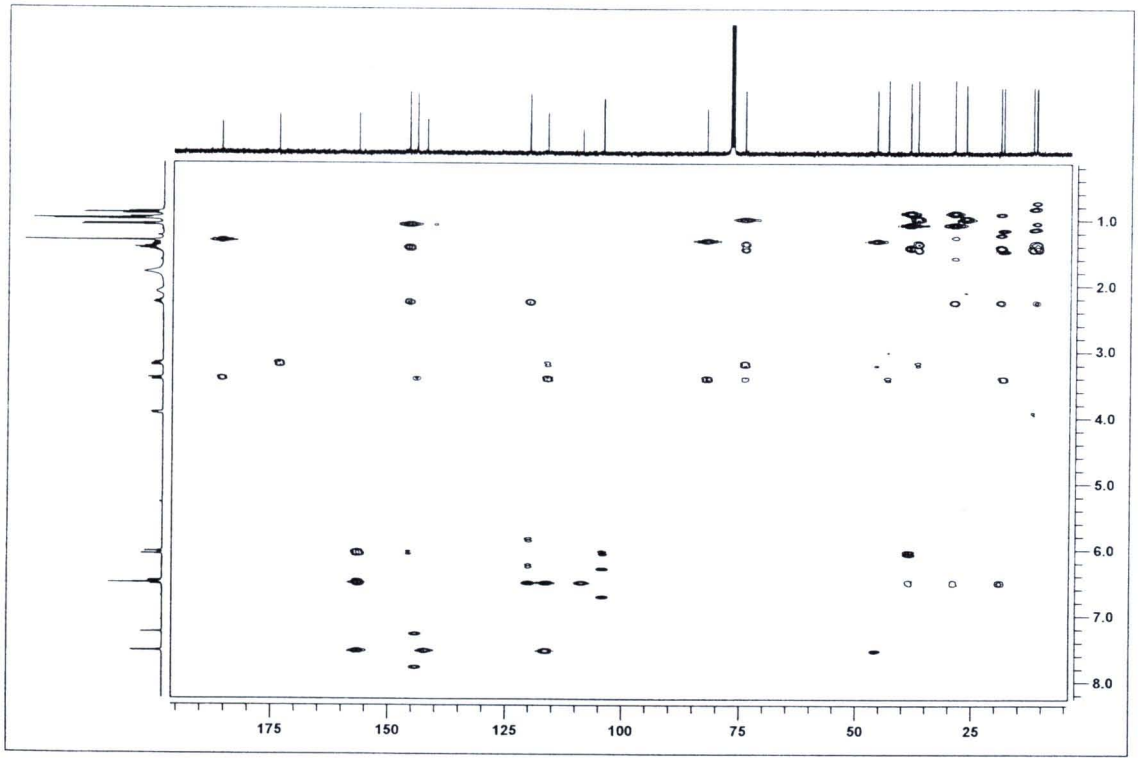

Figure 133 HMBC spectrum of chaetoviridin G (**3.7**).

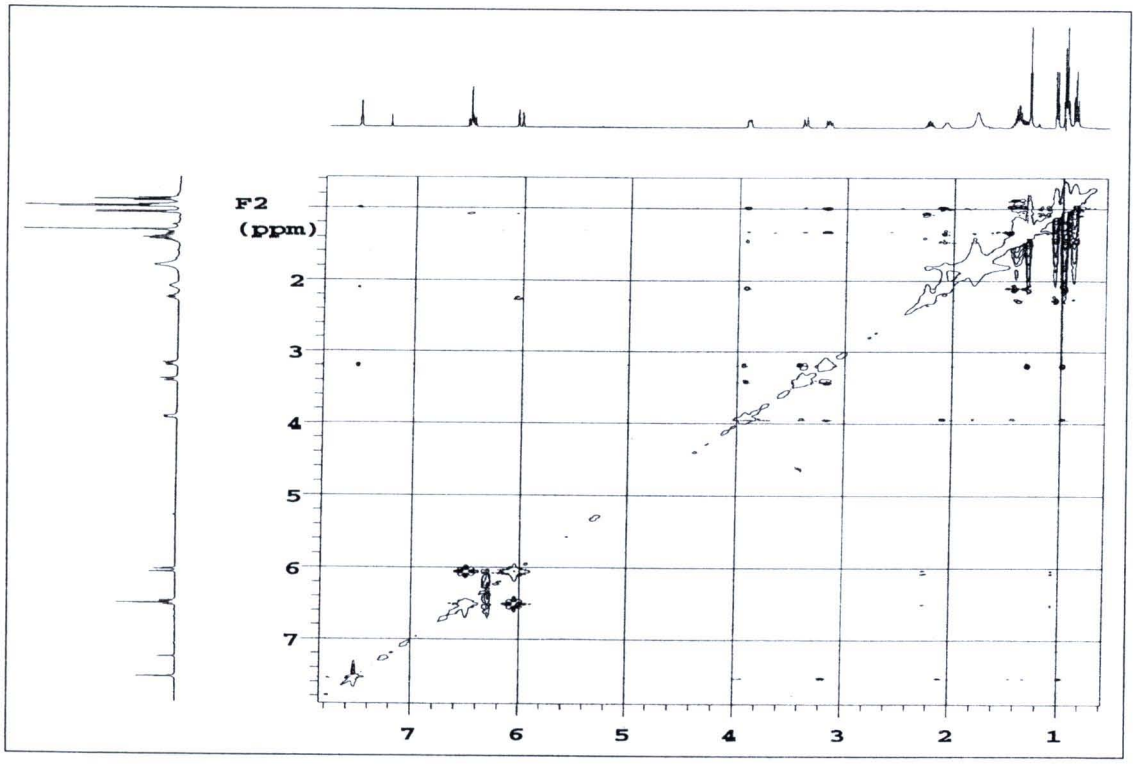

Figure 134 NOESY spectrum of chaetoviridin G (**3.7**).

RESEARCH PUBLICATIONS

Publication:

1. Khumkomkhet P, Kanokmedhakul S, Kanokmedhakul K, Hahnvajanawong J, Soytong K. Antimalarial and Cytotoxic Depsidones from the Fungus *Chaetomium brasiliense*. **J. Nat. Prod**. 2009; 72:1487-1491.

Oral Presentation:

1. Khumkomkhet P, Kanokmedhakul S, Kanokmedhakul K, Hahnvajanawong J, Soytong K, "Bioactive Compounds from the Fungus *C. brasiliense*", at the 4th Annual Meeting of Thai Mycological Association and Mycology Conference in Thailand, Maejo University, Changmai, Thailand, 24 October, 2009.
2. Khumkomkhet P, Kanokmedhakul S, Kanokmedhakul K, Hahnvajanawong J, Soytong K, "Chemical Constituents and Their Bioactivities from the Fungus *Chaetomium brasiliense*", at the 1st Annual Meeting and Research of Thailand, at Roi Et Rajabhat university, Roi Et, Thailand, 18 March,2010.

Poster Presentation

1. Khumkomkhet P, Kanokmedhakul S, Kanokmedhakul K, Hahnvajanawong J, Soytong K, "Cytotoxicity Principles from the Fungus *C. Brasiliense*" at the 6th International Congress for innovation in chemistry (PERCH-CIC Congress VI), Jomtien Plam Beach Resort Pattaya, Chonburi, Thailand, 3 May 2009.
2. Khumkomkhet P, Kanokmedhakul S, Kanokmedhakul K, Hahnvajanawong J, Soytong K, "Chemical Constituents from *Chaetomium brasiliense* ", at the 3rd Annual Meeting of Thai Mycological Association and Mycology Conference in Thailand, Faculty of Agriculture, Khon Kaen University, Khon Kaen, Thailand, 11 October 2008.

J. Nat. Prod. **2009**, *72*, 1487–1491 1487

Antimalarial and Cytotoxic Depsidones from the Fungus *Chaetomium brasiliense*

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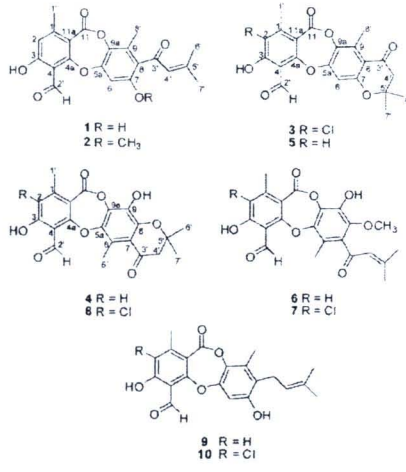
Four new depsidones, mollicellins K–N (**1**–**4**), and six known depsidones, mollicellins B (**5**), C (**6**), E (**7**), F (**8**), H (**9**), and J (**10**), along with two known sterols were isolated from the fungus *Chaetomium brasiliense*. Their structures were elucidated on the basis of 1D and 2D NMR spectroscopic data and chemical transformation. Among these isolates, **1**–**3**, **5**–**7**, and **10** exhibited antimalarial activity against *Plasmodium falciparum*. Only **1** exhibited antimycobacterial activity against *Mycobacterium tuberculosis* and antifungal activity against *Candida albicans* using in vitro assays. In addition, **1**–**10** showed cytotoxicity against the KB, BC1, NCI-H187, and five cholangiocarcinoma cell lines.

The fungus *Chaetomium brasiliense* is one of ca. 22 *Chaetomium* species that have been found in Thailand.[1,2] Previous investigations on secondary metabolites from *Chaetomium* species resulted in the isolation of compounds such as benzoquinone derivatives,[3] tetra-*S*-methyl derivatives,[4] azaphilones,[5–7] bis-azaphilones[7] indol-3-yl-[13]cytochalasans, and chaetoglobosin analogues.[8–14] In addition, anthraquinone-chromanone,[11] orsellinic acid, and globosumones[15] have also been reported. *Chaetomium brasiliense*[16] has been reported to produce chaetochalasin A[17] and four depsidones, mollicellins D, H, I, and J.[18] As part of our work on bioactive constituents from *Chaetomium* species, we noted that hexane and EtOAc extracts of *C. brasiliense*, a strain isolated from Thai soil, showed in vitro antimalarial activity against *Plasmodium falciparum* (IC_{50} 3.0 and 2.9 μg/mL, respectively), and the EtOAc extract also showed antimycobacterial activity against *Mycobacterium tuberculosis* (MIC 50 μg/mL). We report herein the isolation, structural characterization, and bioactivity of four new depsidones (**1**–**4**), six known depsidones (**5**–**10**), and two known sterols from *C. brasiliense*.



Results and Discussion

Depsidones **1**–**10** and two sterols were isolated as solids from hexane, EtOAc, and MeOH extracts of dried mycelial mat of *C. brasiliense* using a combination of silica gel column chromatography (CC) and preparative TLC. Structures of the known compounds were identified by physical and spectroscopic data measurements (IR, ^{1}H and ^{13}C NMR, 2D NMR, and MS) and by comparing the data obtained with published values, as 24(*R*)-5α,8α-epidioxyergosta-6,22-diene-3β-ol,[17] ergosterol,[19] and mollicellins B, C, E, F (**5**–**8**),[20] H and J (**9** and **10**).[18] The details of physical properties and spectroscopic data of mollicellins B, C, E, and F (**5**–**8**)[20] are also presented, since they have not yet been reported.

Compound **1** was obtained as a white solid, and its molecular formula, $C_{31}H_{38}O_7$, was deduced from the HRESITOFMS (observed *m/z* 383.1161 $[M + H]^+$), indicating 13 degrees of unsaturation. The IR spectrum showed the presence of OH (3407 cm^{-1}), carbonyl ester (1731 cm^{-1}), aromatic aldehyde (1656 cm^{-1}), α,β-unsaturated ketone (1638 cm^{-1}), and aromatic (1594 cm^{-1}) groups. The ^{13}C NMR and DEPT spectra (Table 1) indicated 21 signals attributable to 13 sp^2 quaternary (including two carbonyl groups), four sp^3 methine (including an aldehyde group), and four methyl carbons. The ^{13}C NMR data together with the degrees of unsaturation revealed that **1** contained two aromatic rings in the molecule. The IR absorption band at 1731 cm^{-1} and the ^{13}C NMR resonance signal at δ 163.7 suggested the presence of a conjugated carbonyl ester group.[18,21] The ^{1}H NMR data showed two singlet signals of aromatic protons at δ 6.72 (H-2) and 6.69 (H-6), as well as two aromatic methyl substituents at δ 2.51 (H_3-1′) and 2.53 (H_3-8′). The low-field singlet signal (δ 12.06) was assigned as a chelated OH involving the carbonyl of an aldehyde group (δ 10.53) at the *ortho* position. The ^{1}H and ^{13}C NMR spectroscopic data of **1** were comparable to an analogue, mollicellin H (**9**),[18] except for the prenyl group at C-8, which was replaced by a 1-oxo-3-methylbut-2-enyl moiety. This unit was deduced from the ^{1}H and ^{13}C NMR signals at δ_H 6.31 (s, H-4′), 2.23 (s, Me-6′), and 2.01 (s, Me-7′) and δ_C 196.0 (C-3′), 126.0 (C-4′), 158.3 (H-5′), 21.5 (Me-6′), and 28.1 (Me-7′), and it was located at C-8 on the basis of the HMBC correlations of H-8′ to C-8, C-9, C-9a, and C-3′, and H-6 to C-5a, C-7, C-8, C-9a, and C-3′. The HMBC spectrum of **1** also showed correlations of H-1′ to C-1, C-2, C-11, C-4a, and C-11a; H-2 to C-3, C-4, C-11a, C-1′, C-4a, and C-11; the OH proton at C-3 to

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Table 1. ^{1}H NMR Data (δ, ppm) of Compounds **1**–**8** in $CDCl_3$

position	1	2	3	4	5	6	7	8
2	6.72 (s)	6.71 (s)		6.72 (s)	6.71 (s)	6.71 (s)		
6	6.69 (s)	6.57 (s)	6.66 (s)		6.66 (s)			
1′	2.51 (s)	2.52 (s)	2.60 (s)	2.53 (s)	2.52 (s)	2.51 (s)	2.57 (s)	2.53 (s)
2′	10.53 (s)	10.60 (s)	10.54 (s)	10.85 (s)	10.53 (s)	10.83 (s)	10.81 (s)	10.78 (s)
4′	6.31 (s)	6.19 (s)	2.68 (s)	2.74 (s)	2.67 (s)	6.25 (s)	6.24 (s)	2.68 (s)
6′	2.23 (s)	2.20 (s)	1.41 (s)	1.47 (s)	1.41 (s)	2.23 (s)	2.23 (s)	1.40 (s)
7′	2.01 (s)	1.93 (s)	1.41 (s)	1.47 (s)	1.41 (s)	1.96 (s)	1.96 (s)	1.40 (s)
8′	2.53 (s)	2.23 (s)	2.67 (s)	2.59 (s)	2.66 (s)	2.17 (s)	2.16 (s)	2.52 (s)
OH-3	12.06 (s)	12.01 (s)	12.68 (s)	12.19 (s)	12.03 (s)	12.17 (s)	12.75 (s)	12.77 (s)
OH-7	10.88 (s)							
OMe-7		3.76 (s)						
OMe-8						3.73 (s)	3.72 (s)	
OH-9				5.67 (s)		5.84 (s)		5.64 (s)

Table 2. ^{13}C NMR Data (δ, ppm) of Compounds **1**–**8** in $CDCl_3$

position	1	2	3	4	5	6	7	8
1	153.4	154.3	150.3	153.2	153.6	153.1	149.8	149.8
2	117.8	118.2	121.1	117.9	117.9	117.7	121.3	121.1
3	165.3	165.7	161.0	165.3	165.2	165.2	161.2	161.0
4	110.7	111.2	110.6	111.0	110.7	110.9	110.8	110.9
4a	161.6	162.3	161.2	163.7	161.5	161.4	160.9	161.3
5a	153.5	151.0	154.7	137.5	154.7	140.2	140.0	137.3
6	106.8	101.6	107.5	122.6	107.5	134.0	134.2	122.6
7	158.3	153.8	158.6	115.8	158.6	117.5	117.4	115.9
8	122.3	129.4	117.2	146.2	117.0	141.2	141.2	146.2
9	131.1	131.8	134.4	142.0	134.3	139.2	139.3	142.0
9a	135.8	137.1	136.5	135.4	136.7	138.7	138.8	135.4
11	163.7	165.2	161.3	161.5	163.5	164.5	162.2	161.4
11a	112.5	113.3	114.0	112.6	112.5	112.7	114.2	114.1
1′	22.8	22.8	19.7	22.1	22.2	22.1	19.5	19.5
2′	192.6	193.3	192.5	195.4	192.6	193.4	193.3	195.1
3′	196.0	194.6	192.5	192.0	192.5	195.4	195.2	191.9
4′	126.0	126.0	50.1	50.4	50.1	125.2	125.1	50.4
5′	158.6	158.1	79.5	80.9	79.3	159.1	159.3	81.1
6′	21.5	21.6	26.3	26.4	14.2	21.1	21.2	26.4
7′	28.1	28.5	26.3	26.4	14.2	28.0	28.0	26.4
8′	16.3	13.5	14.2	13.1	26.3	12.1	12.1	13.0
OMe-7		56.8						
OMe-863.1						63.1	63.1	

C-2, C-3, and C-4; H-6 to C-5a, C-7, C-8, and C-9a; the aldehyde proton (H-2′) to C-3 and C-4; the OH proton at C-7 to C-6, C-7, and C-8; H-4′ to C-3′, C-6′, and C-7′; H-6′ to C-4′, C-5′, C-7′, and C-3′; and H-7′ to C-4′, C-5′, and C-6′ to confirm the connectivity in the molecule (Figure 1). Surprisingly, the ^3J correlation of the aldehyde proton (H-2′) to C-4a was not observed in the HMBC experiment. Thus, the chemical shift of C-4a was then identified by comparison with those reported for the analogues mollicellins I and J[18] and also from the ^4J correlations of H-2 and H-1′ in the HMBC spectrum. In addition, the NOESY spectrum of **1** demonstrated correlations between aldehyde proton H-2′ and H-6, between H-1′ and H-2, and from H-4′ and H-8′ to H-7′ (Figure 1). Chemical transformation of **1** by cyclization with MeOH in the presence of *p*-toluenesulfonic acid yielded the product that was identical (mp, IR, NMR, and behavior on TLC) to natural mollicellin B (**5**) (Tables 1 and 2). On the basis of the above data, the structure of **1** was defined as a new depsidone and has been named mollicellin K.

Compound **2** was obtained as a white solid, and its molecular formula, $C_{22}H_{30}O_7$, was deduced from HRESITOFMS (observed *m/z* 397.1286 $[M + H]^+$), indicating 13 degrees of unsaturation. The IR spectrum showed the presence of OH (3439 cm^{-1}), carbonyl ester (1729 cm^{-1}), aromatic aldehyde (1677 cm^{-1}), α,β-unsaturated ketone (1644 cm^{-1}), and aromatic (1608 cm^{-1}) groups. The ^{1}H and ^{13}C NMR spectra of **2** were similar to those of **1**, except for the OH group at C-7, which was substituted by an OCH_3 group (δ_H 3.76, δ_C 56.8). The complete assignments of the ^{1}H and ^{13}C NMR signals of **2** were established from the DEPT, COSY, HSQC, HMBC, and NOESY data (Tables 1 and 2). The NOESY spectrum of **2** showed correlations between an aldehyde proton (H-2′) and H-6, H-6, and the OCH_3 protons at C-7 to support the structure of **2**. Thus, **2** was defined as a new depsidone and has been named mollicellin L.

Compound **3** was obtained as a white solid, $C_{21}H_{17}ClO_7$, as deduced from HRESITOFMS (observed *m/z* 439.0561 $[M + Na]^+$ and its ^{37}Cl isotope *m/z* 441.0601 $[M + 2 + Na]^+$), implying 13 degrees of unsaturation. The IR spectrum of **3** showed characteristics of OH (3454 cm^{-1}), ester carbonyl (1736 cm^{-1}), aromatic aldehyde (1688 cm^{-1}), conjugated ketone (1652 cm^{-1}), and aromatic (1600 cm^{-1}) groups. The ^{13}C NMR and DEPT spectra revealed 21 signals attributable to 13 sp^2 quaternary (including two carbonyl groups), one sp^3 quaternary, two sp^2 methine (including an aldehyde group), one sp^3 methylene, and four methyl carbons. From these data, **3** contained two aromatic rings and a conjugated carbonyl ester as described in **1**. The ^{1}H NMR spectrum of **3** (Table 1) showed only one aromatic singlet signal at δ 6.66 (H-6) and two aromatic methyl substituents at δ 2.60 (H-1′) and 2.68 (H-8′), which were different from **1**. The 1-oxo-3-methylbut-2-enyl moiety at C-8

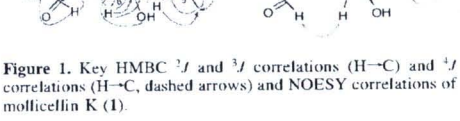

Figure 1. Key HMBC ^2J and ^3J correlations (H→C) and ^4J correlations (H→C, dashed arrows) and NOESY correlations of mollicellin K (**1**).

Table 3. Biological Activities of the Isolated Compounds

compound	antimalarial (IC_{50}, μg/mL)	anti-TB (MIC, μg/mL)	antifungal (IC_{50}, μg/mL)	cytotoxicity (IC_{50}, μg/mL)		
				KB[a]	BC1[b]	NCI-H187[c]
1	1.2	12.5	1.2	1.9	6.8	0.35
2	3.4	inactive	inactive	33.9	nd	9.5
3	2.9	inactive	inactive	Inactive	inactive	0.68
4	inactive	inactive	inactive	25.9	nd	13.5
5	4.7	inactive	inactive	37.1	nd	14.7
6	9.1	inactive	49.9	46.3	inactive	3.1
7	3.2	inactive	39.7	nd	nd	1.0
8	inactive	inactive	nd	37.9	nd	13.1
9	nd	inactive	nd	16.6	nd	3.9
10	4.9	inactive	nd	29.1	nd	23.3
artmisinin	0.001					
isoniazid		0.05				
kanamycin sulfate		2.5				
amphotericin B			0.034			
ellipticine				0.36	0.26	0.32

[a] Human epidermoid carcinoma of the mouth. [b] Human breast cancer. [c] Human small cell lung cancer. nd = not determined. Inactive at >50 μg/mL.

in **1** was replaced by a dihydropyrone ring fused to an aromatic ring, as shown by the signals of two geminal methyl groups both at δ 1.41 (H-6′ and H-7′) and one methylene group at δ 2.67 (s, H-4′). The low-field singlet signal at δ 12.68 was assigned as an OH chelated to an aldehyde carbonyl group (δ 10.54) at the *ortho* position as in **1**. The structure of **3** was constructed by a combination of 2D NMR analyses. The HMBC spectrum demonstrated correlations of H-1′ to C-1, C-2, C-11, C-4a, and C-11a; the OH proton at C-3 to C-2, C-3, and C-4; H-6 to C-5a, C-7, C-8, and C-9a; the aldehyde proton (H-2′) to C-3 and C-4; H-4′ to C-8, C-3′, C-5′, C-6′, and C-7′; H-6′ to C-4′, C-5′, and C-7′; H-7′ to C-4′, C-5′, and C-6′; and H-8′ to C-7, C-5a, C-8, C-9, C-3′, and C-9a (Figure 2). In addition, the Cl−C(2) was determined by comparing its ^{13}C NMR spectrum with those reported for mollicellins J,[18] K (**1**), and B (**5**), as well as the HMBC correlation of H-1′ to C-2 (δ_C 121.1). The NOESY spectrum of **3** also supported the structure via the correlations between H-2′ and H-6 and between H-4′ and H-6′ and H-7′ (Figure 3) On the basis of the above data, the structure of **3** was defined as a new depsidone, and it has been named mollicellin M.

Compound **4** was obtained as a white solid, and its molecular formula, $C_{31}H_{18}O_8$, was deduced from HRESITOFMS (observed *m/z* 421.0897 [M + Na]$^+$), implying 13 degrees of unsaturation. The IR spectrum of **4** indicated OH (3355 cm^{-1}), ester carbonyl (1738 cm^{-1}), conjugated aldehyde (1688 cm^{-1}), conjugated ketone

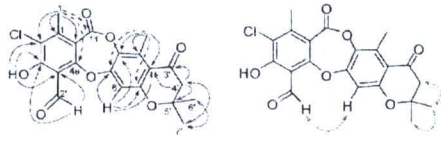

Figure 2. Key HMBC ^2J and ^3J correlations (H→C) and ^4J correlations (H→C, dashed arrows) and NOESY correlations of mollicellin M (**3**).

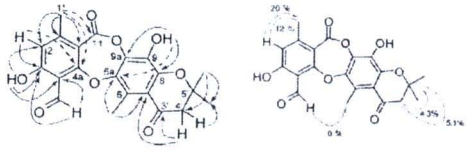

Figure 3. Key HMBC ^2J and ^3J correlations (H→C) and ^4J correlations (H→C, dashed arrows) and NOE-difference data of mollicellin N (**4**).

Table 4. Biological Activities of the Isolated Compounds against Cholangiocarcinoma

compound	cytotoxicity (IC_{50}, μg/mL)				
	KKU-100[a]	KKU-M139[b]	KKU-M156[c]	KKU-M213[d]	KKU-M214[e]
1	4.46 ± 0.08	13.94 ± 2.87	6.65 ± 1.15	nd	4.92 ± 0.26
3	6.28 ± 0.94	8.55 ± 3.20	6.04 ± 0.15	13.19 ± 1.17	4.51 ± 0.18
4	6.46 ± 1.24	4.34 ± 0.08	2.90 ± 0.07	3.00 ± 0.36	5.05 ± 0.50
5	4.63 ± 0.01	11.66 ± 2.70	15.66 ± 0.88	6.94 ± 1.02	4.50 ± 0.39
6	5.12 ± 0.17	2.51 ± 0.36	4.18 ± 0.11	3.2 ± 0.52	3.35 ± 0.04
7	4.83 ± 0.05	5.03 ± 0.16	5.22 ± 0.08	4.44 ± 0.05	7.81 ± 1.13
8	5.21 ± 0.04	5.21 ± 0.04	5.36 ± 0.15	4.98 ± 0.05	4.40 ± 0.02
ellipticine	7.11 ± 0.09	1.21 ± 0.03	2.02 ± 0.11	0.30 ± 0.001	0.21 ± 0.04

[a] Poorly differentiated adenocarcinoma. [b] Squamous carcinoma. [c] Moderately differentiated adenocarcinoma. [d] Adenosquamous carcinoma. [e] Moderately differentiated denocarcinoma. nd = not determined.

(1644 cm^{-1}), and aromatic (1574 cm^{-1}) groups. The ^{13}C NMR and DEPT spectra revealed 21 signals attributable to 13 sp^2 quaternary (including two carbonyl groups), one sp^3 quaternary, two sp^2 methine (including an aldehyde group), one sp^3 methylene, and four methyl carbons. The ^{1}H and ^{13}C NMR spectra of **4** (Tables 1 and 2) showed splitting patterns similar to those of **3** with four singlet methyl (δ_H 2.53, 2.59, 1.47, and 1.47), one methylene (δ_H 2.74), and two methine groups (δ_H 6.72 and 10.85). However, groups substituted on the aromatic ring and chromone units of **4** were located at different positions than in **3**. The HMBC spectrum exhibited correlations of H-1′ to C-1, C-2, C-4a, C-11, and C-11a; H-2 to C-1, C-3, C-4, C-4a, and C-11a; the OH group at C-3 to C-2, C-3, and C-4; the OH group at C-9 to C-8, C-5a, and C-9a; aldehyde proton H-2′ to C-3 and C-4; H-4′ to C-7, C-3′, C-5′, C-6′, and C-7′; H-6′ to C-4′, C-5′, and C-7′; and H-7′ to C-4′, C-5′, and C-6′, confirming the structure of **4** (Figure 3). The NOESY spectrum of **4** showed correlations between H-2 and H-1′ and between H-4′ and H-6′ and H-7′. Unfortunately, the correlation between aldehyde proton H-2′ and C_3-8′ was not observed and the NOE-difference data showed the same correlations of protons as in the NOESY experiment (Figure 3). This suggested that the distance between the aldehyde proton (H-2′) and C_3-8′ is more than 4.2 Å.[22] On the basis of the above evidence, compound **4** was determined to be a new depsidone, and it was named mollicellin N.

The isolated compounds were tested for their bioactivities at the Bioassay Research Facility of the National Center for Genetic Engineering and Biotechnology (BIOTEC), NSTDA, Thailand, and the results are shown in Table 3. Cytotoxicity tests against cholangiocarcinoma were performed at the Liver Fluke and Cholangiocarcinoma Research Center, Faculty of Medicine, Khon Kaen University, Thailand, and the results are given in Table 4.

Mollicellins K−M (**1**−**3**), B (**5**), C (**6**), E (**7**), and J (**10**) showed antimalarial activity against *Plasmodium falciparum* with IC_{50} ranging from 1.2−9.1 μg/mL. Only **1** showed moderate activity

against *Mycobacterium tuberculosis* (MIC 12.5 μg/mL) and potent activity against *Candida albicans* (1.2 μg/mL), as well as cytotoxicity against KB cells (1.9 μg/mL). However, compounds **1**, **3**, **6**, **7**, and **9** exhibited significant cytotoxicity against NCI-H187 cell lines with IC_{50} values of 0.35, 0.68, 3.1, 1.0, and 3.9 μg/mL, respectively (Table 3). In addition, compounds **1** and **3**–**8** exhibited significant cytotoxicity against five cholangiocarcinoma cell lines (KKU-100, KKU-M139, KKU-M156, KKU-M213, and KKU-M214) with IC_{50} values ranging from 2.5 to 15.7 μg/mL. It should be noted that all compounds exhibited IC_{50} values against KKU-100 ranging from 4.5 to 6.5 μg/mL and were more cytotoxic than the control drug ellipticine (Table 4).

The antimalarial and antimycobacterial activities of the isolated compounds corresponded to the preliminary screening tests for the crude extracts. Among the seven depsidones that exhibited antimalarial activity, mollicelline K (**1**) was more active than its crude extracts. In addition, mollicelline K (**1**) was the only one that exhibited antimycobacterial activity and was also more potent than crude extracts. Moreover, of the compounds that were tested for cytotoxicity against several cancer cell lines, most of them showed significant cytotoxicity, especially against cholangiocarcinoma cells.

Experimental Section

General Experimental Procedures. Melting points were determined using a Gallenkamp melting point apparatus and were uncorrected. UV spectra were measured on an Agilent 8453 UV–visible spectrophotometer. IR spectra were taken on a Perkin-Elmer Spectrum One spectrophotometer. NMR spectra were recorded in $CDCl_3$ on a Varian Mercury Plus 400 spectrometer, using residual $CHCl_3$ as an internal standard. HRESITOFMS were recorded on a Micromass Q-TOF-2 spectrometer. Column chromatography and preparative TLC were carried out on silica gel 60 (230–400 mesh) and PF_{254}, respectively.

Fungal Material. The fungus *C. brasiliense* was collected from Doi Inthanon, Jomtong District, Chiangmai Province, Thailand, in June 2006 and was identified by K.S. A voucher specimen (no. Chbr01) was deposited at the Department of Plant Pest Management, King Mongkut's Institute of Technology Ladkrabang, Bangkok, Thailand. The fungus was cultured in conical flasks (1 L, 65 flasks) with potato dextrose broth (PDB) (200 mL/flask) and incubated in standing condition at 25–28 °C for 4 weeks. The culture broth was filtered to give a wet mycelial mat and then air-dried at room temperature.

Extraction and Isolation. The air-dried mycelial mat (300 g) was ground and extracted successively at room temperature with hexane (700 mL × 3), EtOAc (700 mL × 3), and MeOH (700 mL × 3) to give crude hexane (6.8 g), EtOAc (17.8 g), and MeOH (20.6 g) extracts. CH_2Cl_2 (35 mL)–hexane (300 mL) was added to the hexane extract to give a solid (95 mg), which was recrystallized from EtOAc–hexane to give mollicellin B (**5**) (34 mg). The filtrate was evaporated to yield a residue, which was subjected to silica gel flash column chromatography (FCC), eluted with a gradient system of hexane–EtOAc to give six fractions, F_1–F_6. The solid in fraction F_2 was recrystallized from EtOAc–hexane to give 24(*R*)-5α,8α-epidioxyergosta-6,22-dienc-3β-ol (74 mg). The filtrate was evaporated to yield a residue, which was further subjected to silica gel FCC eluted with a gradient system of hexane–EtOAc to give ergosterol (104 mg). Fraction F_3 was purified by preparative TLC using 20% EtOAc–hexane to give mollicellin E (**7**) (24 mg). Fraction F_4 was rechromatographed by FCC, eluted with 20% EtOAc–hexane, to afford additional mollicellin B (**5**) (26.3 mg) and mollicellin K (**1**) (43 mg). Fraction F_5 was purified by silica gel FCC, eluted with a gradient of hexane–EtOAc to give four subfractions, $F_{5.1}$–$F_{5.4}$. Subfraction $F_{5.2}$ was subjected to silica gel FCC, eluted with a gradient of hexane–EtOAc, to give mollicellin L (**2**) (18 mg). Fraction F_6 was purified by silica gel FCC, eluted with a gradient of hexane–EtOAc, to give subfractions $F_{6.1}$–$F_{6.4}$. Subfraction $F_{6.1}$ was rechromatographed by FCC, eluted with 20% EtOAc–hexane, to yield additional amounts of mollicellin B (**5**) (26.3 mg) and mollicellin K (**1**) (45 mg). Fraction $F_{6.3}$ was rechromatographed by FCC, eluted with 40% EtOAc–hexane to give additional mollicellin E (**7**) (31.1 mg).

The EtOAc extract (17.8 g) was initially subjected to silica gel FCC, eluted with the same gradient system as the hexane extract above to give 10 fractions, $F1/2_1$–$F1/2_{10}$. Fraction $F1/2_1$ was subjected to silica gel FCC, eluted with a gradient of hexane–EtOAc, to give mollicellin J (**10**) (54 mg), an additional amount of mollicellin E (**7**) (15.3 g), and mollicellin N (**4**) (6 mg). Fraction $F1/2_4$ was separated by FCC, eluted with a gradient of hexane–EtOAc, to yield additional mollicellin K (**1**) (67 mg) and mollicellin B (**5**) (30 mg). Fraction $F1/2_5$ was subjected to FCC, eluted with a gradient of hexane–EtOAc, to give mollicellin C (**6**) (13.2 mg), mollicellin B (**5**) (10 mg), mollicellin M (**3**) (7.8 mg), and mollicellin N (**4**) (16 mg). Fraction $F1/2_6$ was separated by silica gel FCC, eluted with a gradient of hexane–EtOAc, to give three subfractions, $F1/2_{6.1}$–$F1/2_{6.3}$. Subfraction $F1/2_{6.1}$ was rechromatographed by FCC, eluted with 40% EtOAc–hexane, to afford additional mollicellin L (**2**) (6.3 mg). Subfraction $F1/2_{6.3}$ was rechromatographed by FCC, eluted with 50% EtOAc–hexane, to yield mollicellin H (**9**) (14 mg). Fraction $F1/2_7$ was further purified by silica gel FCC, eluted with a gradient of hexane–EtOAc, to give three subfractions, $F1/2_{7.1}$–$F1/2_{7.3}$. Subfraction $F1/2_{7.1}$ was further purified by preparative TLC using 20% EtOAc–hexane as eluent to yield additional mollicellin B (**5**) (15 mg). Subfraction $F1/2_{7.2}$ was rechromatographed by FCC, eluted with 50% EtOAc–hexane, to give mollicellin F (**8**) (21 mg).

The MeOH extract (20.6 g) was subjected to silica gel FCC, eluted with a gradient of hexane–EtOAc and EtOAc–MeOH to yield fractions F'''–F'''_4. Fraction F'''_3 yielded additional mollicellin C (**6**) (7 mg). Fraction F'''_4 afforded additional mollicellin E (**7**) (11.4 mg).

Mollicelline K (1): white solid; mp 178–181 °C; UV (MeOH) λ_{max} (log ε) 203 (4.47), 264 (4.52) nm; IR (KBr) ν_{max} 3407, 2977, 2360, 1731, 1656, 1638, 1594, 1573 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; HRESITOFMS *m/z* 383.1161 $[M + H]^+$ (calcd for $C_{21}H_{19}O_7$ + H, 383.1131).

Mollicelline L (2): white solid; mp 215–219 °C; UV (MeOH) λ_{max} (log ε) 203 (4.27), 264 (4.47) nm; IR (KBr) ν_{max} 3439, 3028, 2983, 2931, 1729, 1677, 1644, 1608, 1568 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; HRESITOFMS *m/z* 397.1286 $[M + H]^+$ (calcd for $C_{21}H_{20}O_7$ + H, 397.1287).

Mollicelline M (3): white solid; mp 247–250 °C; UV (MeOH) λ_{max} (log ε) 201 (4.01), 261 (3.95) nm; IR (KBr) ν_{max} 3454, 2979, 2917, 1736, 1688, 1652, 1600, 1562 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; HRESITOFMS *m/z* 439.0561 $[M + Na]^+$ (calcd for $C_{21}H_{17}ClO_7$ + Na, 439.0561).

Mollicelline N (4): white solid; 251–253 °C; UV (MeOH) λ_{max} (log ε) 201 (3.67), 267 (3.89) nm; IR (KBr) ν_{max} 3355, 2979, 2932, 1738, 1688, 1644, 1574 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; HRESITOFMS *m/z* 421.0897 $[M + Na]^+$ (calcd for $C_{21}H_{18}O_8$ + Na, 421.0899).

Mollicelline B (5): white solid; mp 203–205 °C; UV (MeOH) λ_{max} (log ε) 201 (4.05), 261 (3.95) nm; IR (KBr) ν_{max} 3461, 3089, 2979, 2929, 2854, 1739, 1686, 1651, 1602, 1574 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; HRESITOFMS *m/z* 405.0953 $[M + Na]^+$ (calcd for $C_{21}H_{18}O_7$ + Na, 405.0950).

Mollicelline C (6): white solid; mp 200–202 °C; UV (MeOH) λ_{max} (log ε) 206 (4.21), 267 (3.97) nm; IR (KBr) ν_{max} 3389, 2928, 2358, 1734, 1645, 1559 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESITOFMS *m/z* 435.0648 $[M + Na]^+$ (calcd for $C_{22}H_{20}O_8$ + Na, 435.1055).

Mollicelline E (7): white solid; mp 169–170 °C; UV (MeOH) λ_{max} (log ε) 205 (4.18), 267 (3.80) nm; IR (KBr) ν_{max} 3382, 2921, 2850, 1741, 1651, 1624, 1566 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESITOFMS *m/z* 469.0427 $[M + Na]^+$ (calcd for $C_{22}H_{19}ClO_8$ + Na, 469.0665).

Mollicelline F (8): white solid; 256–257 °C; UV (MeOH) λ_{max} (log ε) 201 (3.71), 267 (3.86), 224 (4.05) nm; IR (KBr) ν_{max} 3400, 2980, 2924, 1741, 1688, 1644, 1565 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESITOFMS *m/z* 455.0318 $[M + Na]^+$ (calcd for $C_{21}H_{17}ClO_8$ + Na, 455.0406).

Cyclization of 1. To a solution of **1** (32.1 mg) in MeOH (5 mL) was added *p*-toluenesulfonic acid (9.4 mg), and the solution was stirred at 50 °C for 4 h. Cooled water was added to the reaction mixture, and it was extracted with EtOAc (10 mL × 3). The organic layer was combined, washed with water and brine, and dried over anhydrous Na_2SO_4. The filtrate was evaporated to dryness, and the residue was separated by preparative TLC (10% EtOAc–hexane) to give **5** (29.2 mg, 91%); mp 202–204 °C; IR and NMR spectra were identical to those of mollicellin B (**5**) (Tables 1 and 2).

Antimalarial Assay. Antimalarial activity was evaluated against the parasite *Plasmodium falciparum* (K1, multidrug-resistant strain), using the method of Trager and Jensen.[23] Quantitative assessment of activity in vitro was determined by means of the microculture radioisotope

technique based upon the method described by Desjardins et al.[24] The inhibitory concentration (IC_{50}) represents the concentration that causes 50% reduction in parasite growth as indicated by the in vitro uptake of [^{3}H]-hypoxanthine by *P. falciparum*. The standard compound was artemisinin (Table 3).

Antimycobacterial Assay. Antimycobacterial activity was assessed against *Mycobacterium tuberculosis* H37Ra using the microplate Alamar Blue assay (MABA).[25] The standard drugs isoniazid and kanamycin sulfate were used as the reference compounds (Table 3).

Antifungal Assay. An antifungal assay was performed against clinical isolated *Candida albicans* using a method modified from the soluble formazan assay described by Scudiero and co-workers.[26] The number of living cells was determined by measuring the absorbance of XTT formazan at 450 nm. The reference substance was amphotericin B (Table 3).

Cytotoxicity Assay. Cytotoxic assays against human epidermoid carcinoma (KB), human breast cancer (BC1), human small cell lung cancer (NCI-H187), and cholangiocarcinoma cell lines were performed employing the colorimetric method as described by Skehan and co-workers.[27] The reference substance was ellipticine (Tables 3 and 4).

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Supporting Information Available: ^{1}H NMR, ^{13}C NMR, and NOESY spectra for mollicellins K–N (**1**–**4**) and B (**5**). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Soytong, K. *Thai Phytopathog.* **1991**, *11*, 86–111.
(2) Petcharat, V.; Soytong, K. *Songklanakarin J. Sci. Technol.* **1991**, *13*, 129–132.
(3) Brewer, D.; Jerram, W. A.; Taylor, A. *Can. J. Microbiol.* **1968**, *14*, 861–866.
(4) Safe, S.; Taylor, A. *J. Chem. Soc., Perkin Trans. 1* **1972**, 472–479.
(5) Takahashi, M.; Koyama, K.; Natori, S. *Chem. Pharm. Bull.* **1990**, *38*, 625–628.
(6) Kanokmedhakul, S.; Kanokmedhakul, K.; Nasomjai, P.; Soytong, K.; Isobe, M.; Kongsaeree, P.; Prabpai, S.; Suksamrarn, A. *J. Nat. Prod.* **2006**, *69*, 891–895.
(7) Phonkerd, N.; Kanokmedhakul, S.; Kanokmedhakul, K.; Soytong, K.; Prabpai, S.; Kongsaeree, P. *Tetrahedron* **2008**, *68*, 9636–9645.
(8) Sekita, S.; Yoshihira, K.; Natori, S. *Tetrahedron Lett.* **1976**, *17*, 1351–1354.
(9) Udagawa, S.; Muroi, T.; Kurata, H.; Sekita, S.; Yoshihira, K.; Natori, S.; Umeda, M. *Can. J. Microbiol.* **1979**, *25*, 170–177.
(10) Probst, A.; Tamm, C. *Helv. Chim. Acta* **1981**, *64*, 2056–2064.
(11) Sekita, S.; Yoshihira, K.; Natori, S.; Kuwano, H. *Chem. Pharm. Bull.* **1982**, *30*, 1629–1638.
(12) Sekita, S.; Yoshihira, K.; Natori, S. *Chem. Pharm. Bull.* **1983**, *31*, 490–498.
(13) Kanokmedhakul, S.; Kanokmedhakul, K.; Phonkerd, N.; Soytong, K.; Kongsaeree, P.; Suksamrarn, A. *Planta Med.* **2002**, *68*, 834–836.
(14) Ding, G.; Song, Y. C.; Chen, J. R.; Xu, C.; Ge, Wang, X. T.; H. M.; Tan, R. X. *J. Nat. Prod.* **2006**, *69*, 302–304.
(15) Bashyal, B. P.; Wijeratne, E. M. K.; Faeth, S. H.; Gunatilaka, A. A. L. *J. Nat. Prod.* **2005**, *68*, 724–728.
(16) Skolko, A. J.; Grove, J. W. *Can. J. Bot.* **1953**, *31*, 779–809.
(17) Oh, H.; Swenson, D. C.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *Tetrahedron Lett.* **1998**, *39*, 7633–7636.
(18) Li, G. Y.; Li, B. G.; Yang, T.; Liu, G. Y.; Zhang, G. L. *Helv. Chim. Acta* **2008**, *91*, 124–129.
(19) Bok, J. W.; Lermer, L.; Chilton, J.; Klingeman, H. G.; Towers, G. H. *Phytochemistry* **1999**, *51*, 891–898.
(20) Stark, A. A.; Kobbe, B.; Buchi, G.; Wogen, G. N.; Demain, A. L. *Appl. Environ. Microbiol.* **1978**, *30*, 412–420.
(21) Chicita, F. C. *Phytochemistry* **1966**, *5*, 815–818.
(22) Pavia, D. L.; Lampman, G. M.; Kriz, G. S.; Vyvyan, J. R. *Introduction to Spectroscopy*, 4th ed.; Books/Cole, Cengage Learning: Belmont, CA, 2008; pp 359–362.
(23) Trager, W.; Jensen, J. B. *Science* **1967**, *193*, 673–675.
(24) Desjardins, R. E.; Canfield, C. J.; Haynes, J. D.; Chulay, J. D. *Antimicrob. Agents Chemother.* **1979**, *16*, 710–718.
(25) Collins, L.; Franzblau, S. G. *Antimicrob. Agents Chemother.* **1997**, *41*, 1004–1009.
(26) Scudiero, D. A.; Shoemaker, R. H.; Paull, K. D.; Monka, A.; Tierney, S.; Nofziger, T. H.; Currens, M. J.; Seniff, D.; Boyd, M. R. *Cancer Res.* **1988**, *48*, 4827–4833.
(27) Skehan, P.; Storeng, R.; Scudiero, D.; Monks, A.; McMahon, J.; Vistica, D.; Warren, J. T.; Bokesch, H.; Kenney, S.; Boyd, M. R. *J. Natl. Cancer Inst.* **1990**, *82*, 1107–1112.

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