International Scholars Journals

African Journal of Botany ISSN: 2314-9825, Vol. 11 (2), pp. 001-006, February, 2023. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Full Length Research Paper

Investigating the potential antidiabetic properties of 7-Methoxycoumarin derived from the bark of marine plant *Rhizophora mucronata*

Andy Ramu* and Veluchamy Vijayakumar

School of Chemistry, Madurai Kamaraj University, Madurai-625021. India

Accepted 21 October, 2022

Coumarin possess a number of biological activity like anticoagulant, antimicrobial, anti-inflammatory, analgesic, antioxidant, anticancer, antiviral, antimalarial etc. But the antidiabetic property of coumarins from marine plants are not attempted so for and hence, the present study has been carried out. The present study isolated a coumarins from the bark of *Rhizophora mucronata.* This coumarins belongs to a group as benzopyrones, which consists of a benzene ring joined to a pyronenucleus and confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral studies. The present work deals with the isolation, characterization and antidiabetic activity of *in vivo* study of this compound. The isolated compounds have been identified as 7- methoxy coumarins and further, the isolated coumarins were subjected for the *in vivo* antidiabetic activity and it reveals that, the 7-methoxy coumarins potentiate antidiabetic activity.

Keywords: 7-methoxycoumarin, marine plant, antidiabetic property, *Rhizophora mucronata.*

INTRODUCTION

It has been estimated that diabetes may affect 439 million adults by 2030, with the major increase occurring in developing countries (Shaw *et al.,* 2010). It is projected that, it will rank as the 9th leading cause of death in low-income countries (Mathers and Loncar, 2006), Venables and Jeukendrup (2009)). There are two major types of diabetes, i.e. type 1 (T1D) or insulin dependent diabetes and type2 (T2D) cornman-insulin in dependent diabetes. The incidence of T2D is reaching epidemic proportions and has been in associated with an increase in obesity (Astrup, 2001; Li, 2003). According to the World Health Organisation (WHO) (Modak *et al.,* 2007) the main complications associated with diabetes are cardiovascular disease and renal failure.

Rhizophora mucronata (Rhizophoraceae) is a mangrove tree. The bark of this plant has been used by the local Thai people in a folk medicine for treatment of nausea, vomiting, diarrhea and stop bleeding in fresh wounds (Boonyapraphat and Chockchaicharaenphorn, 1998). This plant has been proved to possesses diterpenoids (Anjaneyulu *et al.,* 2002), triterpenoids (Ahmed *et al.,* 1998), andsteroids (Ghosh *et al.,* 1985), including alkaloids, pheonolic compounds, coumarins, flavonoids, proteins and sugars, were analyzed by standard protocols (Siddiqui and Ali, 1997).

*Corresponding Author E-mail: ramumkuku@yahoo.co.in

Coumarin, a phenolic compound present in human dietary fruits and vegetables, is known to have antioxidant potential like vitamin E (a-tocopherol) and Vitamin C for antioxidant have lipid lowering potential (Ramesh and Pugalendi, 2005). Derivative of coumarin, is a benzopyrone in nature and is present in the edible fruits, golden apple (*Aeglemarmelos Correa*) (Siddiqui and Ali, 1997), and bitter orange (*Citrus aurantium*) (Amrani *et al.,* 2009). The parent compound coumarin has been reported to reduce blood glucose level (Yen *et al.,* 2003). *Cetto et al*. (2000) have reported that UMB has antioxidant activity (Cetto and Wiedenfeld, 2001), but no detailed study has been carried out on the effect of UMB on blood glucose in streptozotocin (STZ)-diabetic rats. Hence, the present study was designed to investigate the effect of 7-methoxycoumarin on blood glucose of STZ-diabetic rats.

MATERIALS AND METHOD

Fresh sample bark of the *R. mucronata* were collected from the Karangkadu mangrove forest (Latitude 9^0 380' N and Longitude $78^0$570' E) in the Ramanathpuram district on the South East coast of India. Authentication of the plant species was done by Professor K. Kathiresan, Centre of Advanced Study in Marine Biology, Annamalai University, Porto Novo, Tamil Nadu, India. Voucher specimens of the sample has been maintained in the herbarium cabinet facility sponsored by the ICMR, New Delhi. Samples were washed three times with tap water and twice with distilled water to remove adhering salts and associated contaminants.

Dried barks of *Rhizophara mucronata* is pulverized and soaked in ethonal and water mixture (3:1) for one week and filtered by using muslin cloth. Further the extracts are concentrated under vacuum on a rotary evaporator, freeze-dried for solvent free residue and stored at -20^oC until used. Isolation and identication of compound were carried out by the present study by following standard procedure. Increasing polarity 100% n-hexane, n-hexane-EtoAc, 100% EtoAc and 100% EtoH, to yield a number of fraction (fr) and further thin layer chromatographic (TLC) analyses were carried out, Fractions with Rf=0.61 brought maximum concentrations of extracts were subjected for spectral identification *viz.*, NMR, LC-MS.

In vivo of hypoglycemic activity of 7- methoxy coumarins was also carried out by the present study. Male wistar rats and male swiss albino mice were maintained in standard hygienic laboratory conditions temperature around 26^0C, day night cycle consisting of 12 and 12 hours. They were provided water and standard pellet food and water adlibitum. Animals were kept in standard polyprolene cages with hygienic conditions maintained. They were used after having obtained clearance from institutional animal ethics committee in Madurai Kamaraj University, Madurai (Reg no: IRBandEC/04.05.2012).

Induction of diabetes was done in overnight fasted male wistar rats by single intraperitneal injection of streptozotocin, 50 $mg.kg^{-1}$ dissolved in 0.1M cold citrate buffer pH 4.5[19].48 hours after it blood samples were drawn by retro orbital route and blood glucose levels were checked to confirm diabetes (Cetto A, *et al.,*2000). Experiments were carried out with the following treatments (T1-T5) five animals were chosen for each treatment groups.

T1- Group 1- Saline alone (Negative control)

T2 - Group2 –Glibenclamide alone (10$mg.kg^{-1}$ p.o (Positive control))

T3- Group3 - 7-methoxycoumarine (500$mg.kg^{-1}$)

T4- Group4- 7-methoxycoumarine (1000$mg.kg^{-1}$)

Blood samples were withdrawn from retro orbital route at 0, 60,120,180 mins [21] after the drug administration. Measurement of blood samples were done by using blood glucose kit.

RESULTS AND DISCUSSIONS

The infrared spectrum of 7-methoxy coumarin exhibits two strong bands at 1667 and 1340 cm−1, which may be assigned to *v*as(C= O) and *v*s(C= O), respectively. The low carbonyl frequency (1667 cm−1) is presumably due to intermolecular hydrogen bonding of the 7-hydroxyl hydrogen either with O (1) or with O (2). The *v*as(C O) (phenolic) has been assigned at 1561 cm−1 (Boonyapraphat and Chockchaicharaenphorn, 1998) as a very strong band. In the IR spectra of diorganotin (IV) derivatives of umbelliferone, there is a significant shift in *v*as(C O) (phenolic) (1604– 1610 cm−1), which indicates the participation of the phenolic oxygen after the deprotonation of phenolic group in bonding with organotin moiety (Figure1) below.

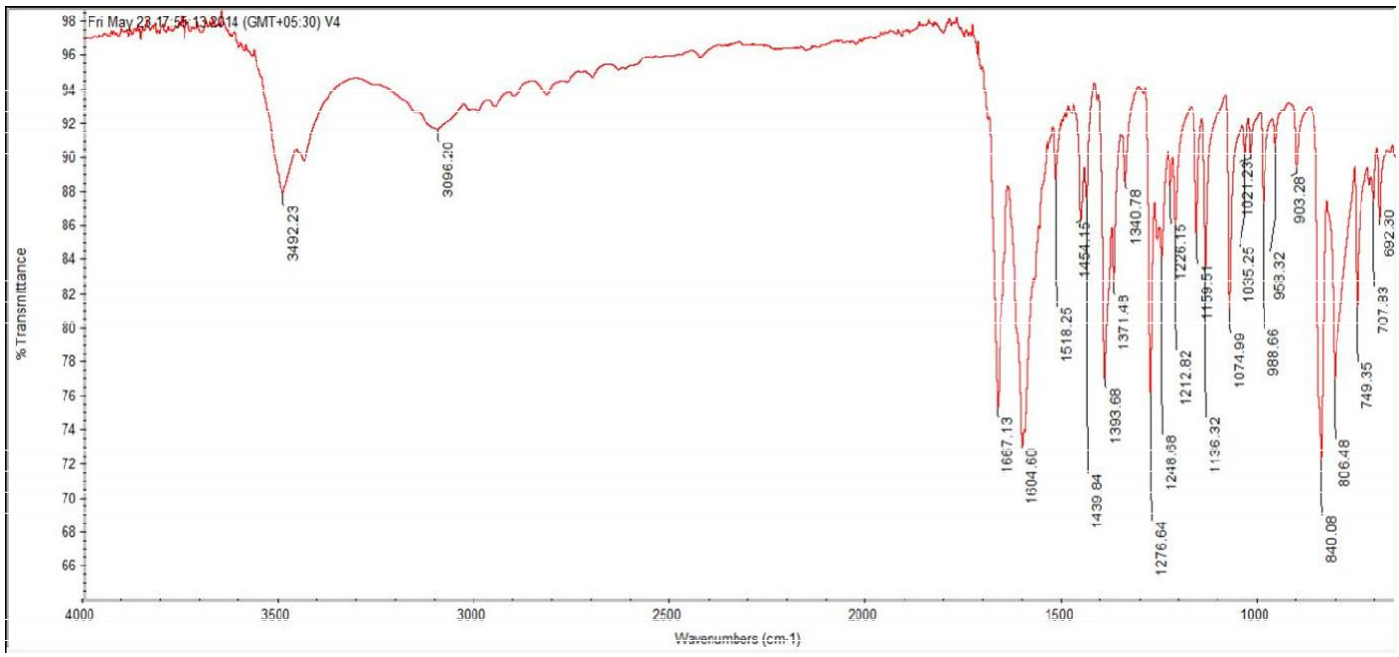

Figure 1

In the 1H NMR (300MHz DMSO-d6) spectrum of the compound, six distinct peaks were observed. A broad singlet at d 4.53 was assigned to the OH proton. Two doublets at d 6.12 and 7.79 with coupling constant of 9.3 Hz were assigned to the protons attached at the C-3 and C- 4 positions. Similarly, two other doublets, at d 6.73 (J = 8.4 Hz), d 7.39 (J = 8.7 Hz) and a singlet at d 6.64, were assigned to the protons attached to C-6, C-5 and C-8, respectively (Figure 2).

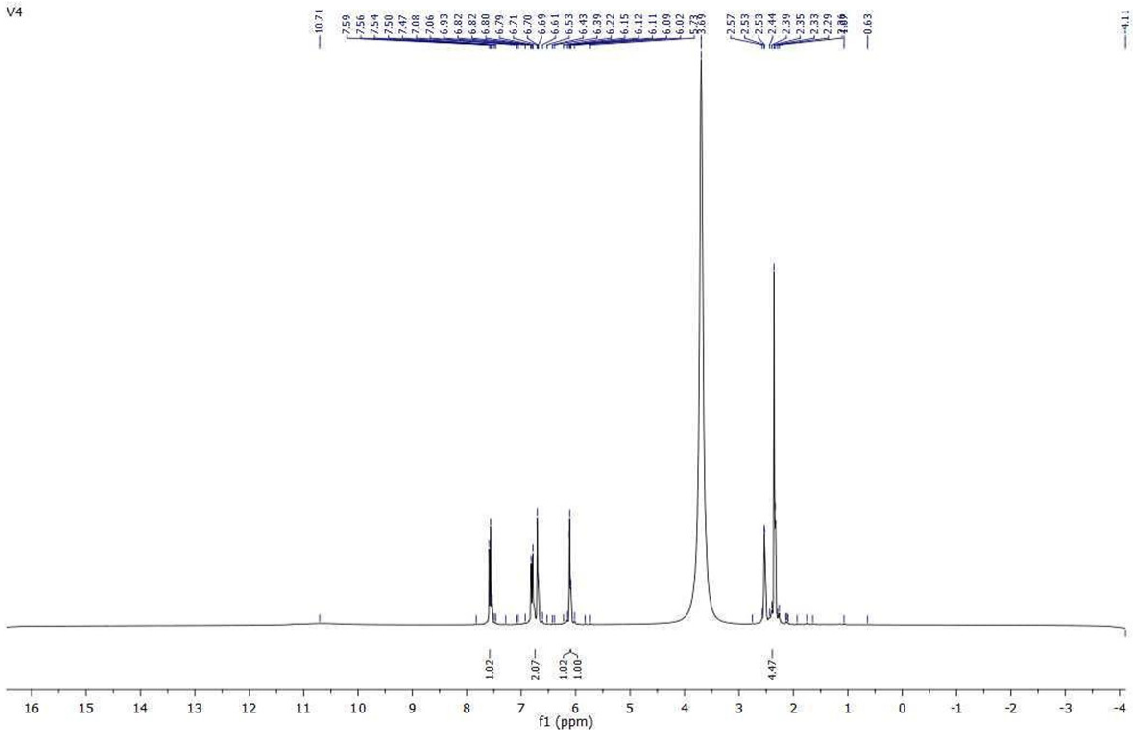

Figure 2

The ^{13}C NMR spectrum of AN-2 showed nine distinct signals. A peak at d 162.3 was assigned to the carbonyl function (C-2) of coumarin derivatives while a downfield signal at d 161.7 revealed the presence of a methoxy function at the C-7 position. Other signals at, d 102.0, 110.9, 111.7, 113.1, 129.2, 144.6 and 155.8 were attributed to C-8, C-3, C-4a, C-6, C-5, C-4 and C-8a, respectively (Figure 3).

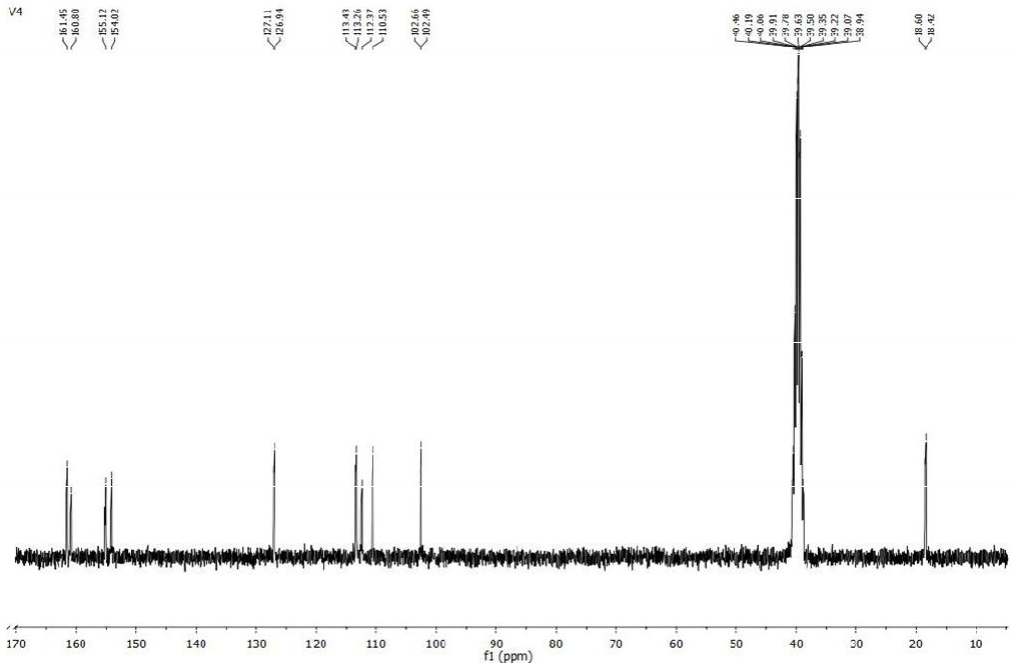

Figure 3

The mass spectra analysis 7- methoxycoumarin, the peak at m/z = 177.08[M+1] amu Na metal adopt in corresponds to the molecular ion peak (Figure 4).

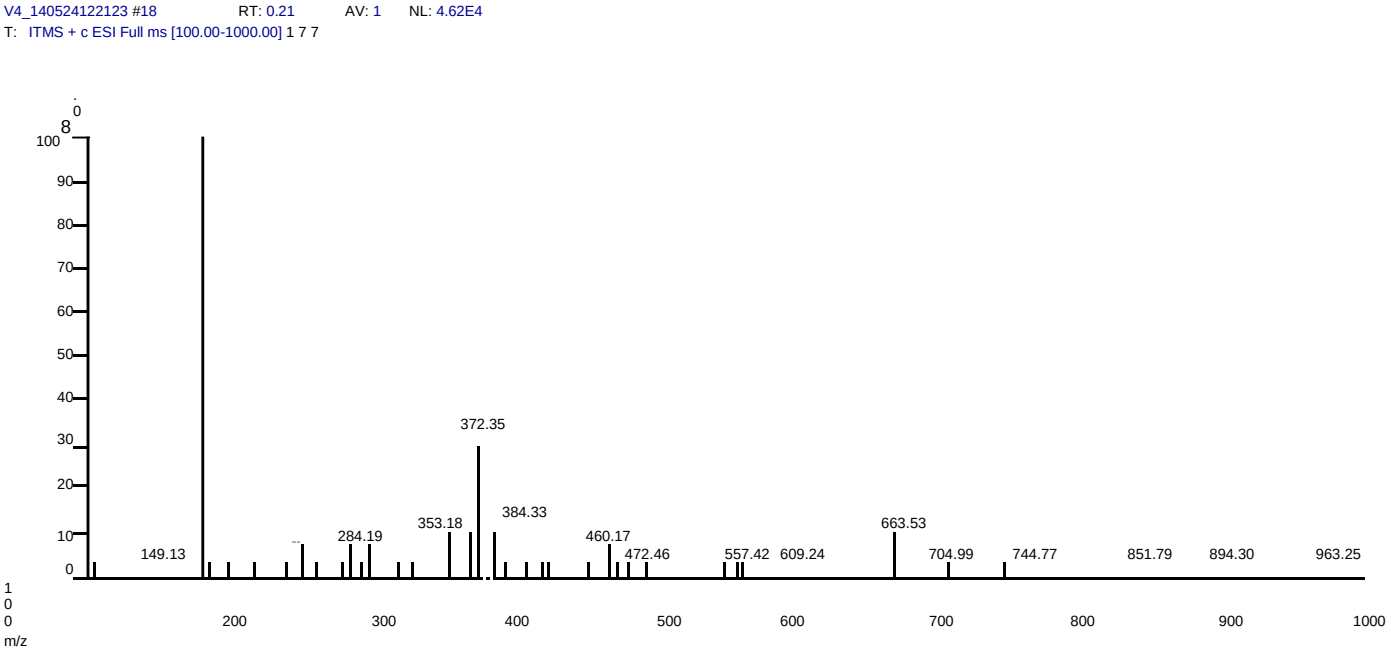

Figure 4

Decreased Glucose level in T2 treated with 7-methoxy coumarine at 500 mg.kg^{-1} concentration.

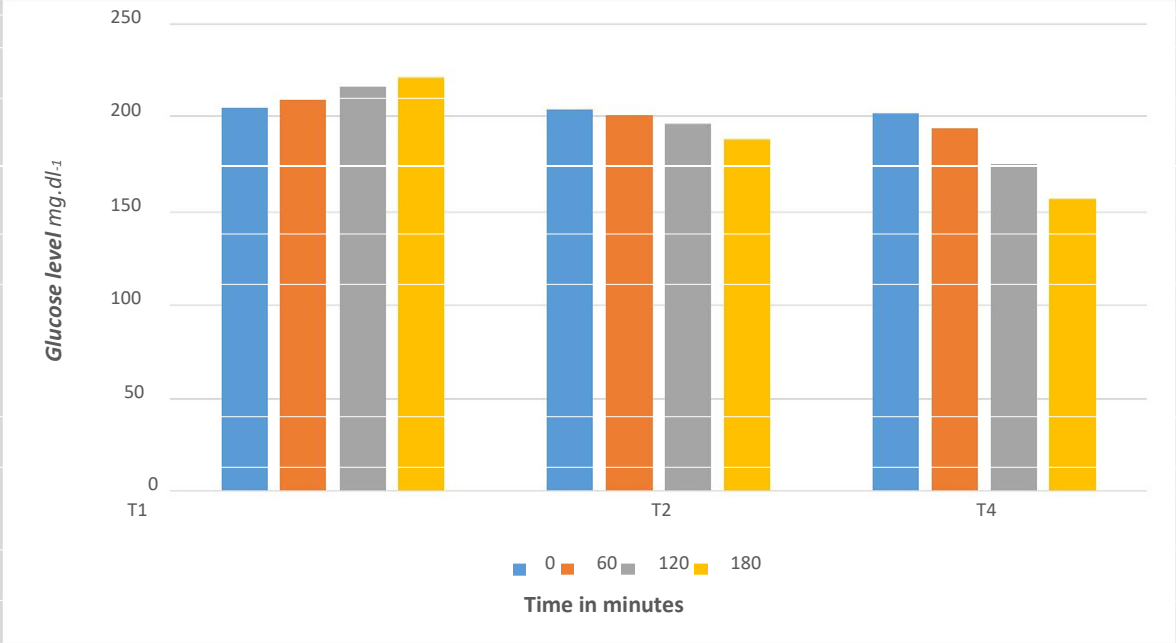

Figure 5

Decreased Glucose level in T3 treated with 7-methoxy coumarine at 1000 mg.kg^{-1} concentration.

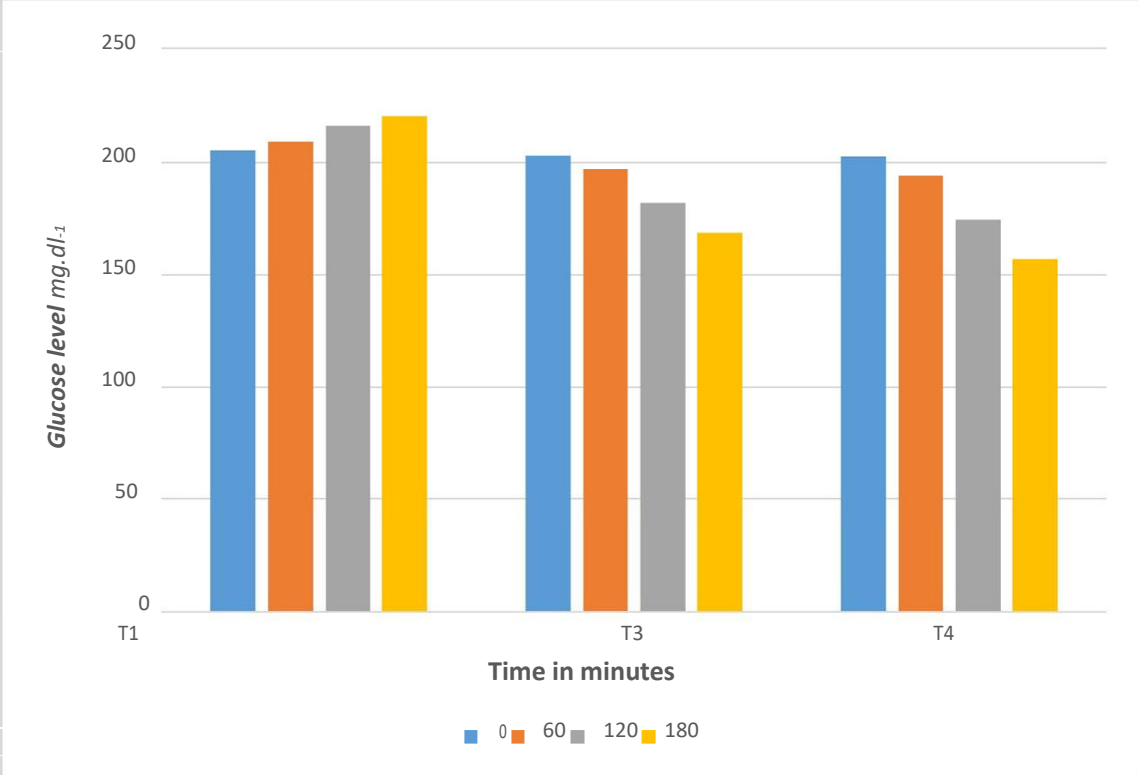

Figure 6

CONCLUSION

Structure prided of (fr-4) compound is 7-methoxy coumarin and anti-diabetic activity studies of both *in vitro* and *in vivo* is more activity. *In vitro* antidiabetic activity was found maximum in the basic medium p^H added with coumarin when compared with the other two p^H (Figures 5-7).

In *in vivo* animal modal, changes in blood glucose level was found normal, diabetic mice with 7-methoxycoumarin compound, Glibenclamide are presented in Figure 8.ral administration of 7-methoxycoumarin ($500mg.kg^{-1}$ and $1000mg.kg^{-1}$) for 1 day showed significant ($p<0.01$).The results of the antidiabetic analysis suggested that, the glucose level decreases (187.6±1.304 in 180 min) in group 3 treated animals, which is highly comparable to the positive control Glibenclamide (157.3±6.39 in 180 min).

ACKNOWLEDGEMENTS

This work is supported by a grant from the UGC-BSR Fund and instrumental facilities given by school of Chemistry, Madurai Kamaraj University, Madurai. I kindly thank to Dr. S. Ravi Kumar, Department of Oceanography and costal area studies to supported biological activity in my work.

REFERENCE

Adityachaudhury N, Ghosh D, Choudhuri A (1974). Coumarin constituents of *Selinumtenuifolium. Phytochem.* 13:235-238.

Ahmed SS, Hiader SI, Rabbani MM (1988). Fitoterapia 59: 79—81

Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra, 1992.31; 173B.

Amrani F, *et al (*2009). *hypoglycaemic* e*ffect* of Thymelaea hirsute in normal and streptozotocin induced diabetic rats, *J. Med. Plant Res.* 3(9): 625-629.

Anjaneyulu ASR, Anjaneyulu V, Rao VL (2002). J. Asian Nat. Prod. Res. 4: 53-61

Astrup A (2001). Healthy lifestyles in Europe: prevention of obesity and type II diabetes bydiet and physical activity. *Public Health Nutrition*. 4: 499–515.

Boonyapraphat N, Chockchaicharaenphorn C (1998). "Thai Medicinal Plants," Vol. II, Prachachon Ltd., Bangkok. pp. 311—312.

Cetto A, Wiedenfeld H (2001). *Hypoglycemic* effect of *Cecropiaobtusifolia* on streptozotocin diabetic rats, *J. ethnopharmacol.* 78: 145-149.

Cetto A, Wiedenfeld H, Revillam M, Sergio A (2000). *Hypoglycemic* effect of *Equisetum myriochaetum*aerial part on streptozotocin diabetic rats. *J. ethnopharmacol.* 72: 129-133.

Deutschländer MS, Van de Venter M, Roux S, Louw J, Lall N (2009). Hypoglycaemicactivity of four plant extracts traditionally used in South Africa for diabetes. *J. Ethnopharmacol.* 124: 619–624.

Erasto P, Adebola PO, Grierson DS, Afolayan AJ (2005). An ethnobotanical study ofplants used for the treatment of diabetes in the Eastern Cape Province, South Africa. *Afr. J. Biotechnol.* 4: 1458–1460.

Ghosh A, Misra S, Dutta AK, Choudhury A (1985). Phytochem. 24: 1725—1727

Hostettmann K, Marston A, Ndjoko K, Wolfender J (2000). The potential of African plants as a source of drugs. *Curr. Organic Chem.* 4: 973–1010.

J. Ethnopharmacol. 103: 261–275.

Kalyani Publishers. pp. 1-5

Li TSC (2003*). Chinese and related North American herbs:phytopharmacology and therapeutic values*, CRC Press, ISBN 1-58716-128-1, Boca Raton, USA.

Madhavan GR, Balraju V, Mallesham B, Chakrabarti R, Lohray VB (2003). Novel coumarin derivatives of heterocyclic compounds as lipid-lowering agents. *Bioorg*. *Med. Chem. Lett*. 13: 2547-2551.

Marles RJ, Farnsworth N (1996). Antidiabetic plants and their active constituents: an Update. *Prof. J. Bot. Med*. 3: 85-135.

Marston AN, Hostet KMA 1995. Malawi Isolation of *antifunga*l and *Larvicidal* constituents of *dzplolophzum buchananz* by centrifugal partition chromatography. *J. natural product. 58(I):128-130*.

Mathers CD, Loncar D (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med.* 3: e442.

Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TPA (2007). Indian herbsand herbal drugs used for the treatment of diabetes. *J. Clin. Biochem. Nutr.* 40: 163–173.

Parmar C, Kaushal MK (1982). *Aeglemarmelos*. In: *Wild Fruits*. New Delhi, India:

Patil AD, Freyer AJ, Eggleston DS, Haltiwanger RC, Bean MF, Taylor PB, Caranfa MJ, Breen AL, Bartus HR, Johnson RK, Hertzberg RP, Westley JW (1993). The inophyllums, novel inhibitors of HIV-1 reverse transcriptase isolated from the Malaysian tree, Calophylluminophyllum Linn. J. Med. Chem. 36: 4131–4138.

Ramesh B, Pugalendi KV (2005). Impact of umbelliferone on erythrocyte redox status in STZ-diabetic rats. *Yale J. Biol. Med*. 78: 133-140.

RazdanTK, Kachroo V, Harkar S, Koul GL (1982). Furanocoumarins from *Heracleumcanescens. Phytochem.* 21:923-927.

Shaw JE, Sicree RA, Zimmet PZ (2010). Global estimates of the prevalence of diabetesfor 2010 and 2030. *Diab. Res. Clin. Pract.* 87: 4–14.

Siddiqui AA, Ali M (1997). Practical pharmaceutical chemistry. 3rded. New Delhi: CBS *Publishers and Distributors*. p. 126 e31.

Singh S, Gupta SK, Sabir G, Gupta MK, Seth PK (2009). A database for anti-diabeticplants with clinical/experimental trials. *Bioinform.* 4: 263–268.

Thring TSA, Weitz FM (2006). Medicinal plant use in the Bredasdorp/Elim region of the Southern Overberg in the Western Cape Province of South Africa.

Venables MC, Jeukendrup AE (2009). Physical inactivity and obesity: links with insulinresistance and type 2 diabetes mellitus. *Diab. Metab. Res. Rev.* 25: S 18-23.

Wu FJ, Sheu SJ (1992). Analysis and processing of Chinese herbal drugs: the study of *Fructus AurantiiImmaturus* (Chin.). *Chin. Pharm. J*. 44: 257-263.

Yen GY, Eisenberg DM, Kaptchuk TJ, Phillips RS (2003). Systematic review of herbsand dietary supplements for glycemic control in diabetes. *Diabetes Care*. 26: 1277–1294.