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Synthesis and bio-evaluation of novel acyl derivatives of karanjin

Anjaneyulu Eanti[a], Madhusudana Kuncha[b], Ande Arundha[b], Sunil Misra[b,d], Siddaiah Vidavalur[c], Sistla Ramakrishna[b,d] & Sanjit Kanjilal[a,d,*]

[a] Centre for Lipid Science and Technology, CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 007, India
[b] Applied Biology Division, CSIR-Indian Institute of Chemical Technology, Tarnaka, Hyderabad 500 007, India
[c] College of Science and Technology, Andhra University, Visakhapatnam 530 003, India
[d] Academy of Scientific and Innovative Research (AcSIR), CSIR-HRDC Campus, Postal Staff College Area Sector 19, Kamla Nehru Nagar, Ghaziabad 201 002, Uttar Pradesh, India
*E-mail: sanjit@iict.res.in

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Different lipidic moieties such as 10-undecenoic, oleic, lipoic, caproic, caprylic and lauric acids have been acylated to demethylated karanjin to prepare six lipoconjugated karanjin. All the derivatives have been evaluated for antimicrobial, anticancer and antiinflammatory activities and compared with karanjin and its demethylated analog. Lipoconjugation does not seem to improve the activity of karanjin against studied bacterial and fungal strains. However, karanjin, demethylated karanjin and six lipoconjugated karanjin show moderate to good anticancer activity against prostate and breast cancer cell lines. Mild antiinflammatory response has also been observed in case of karanjin and lipoic acid-conjugated karanjin.

Keywords: Synthesis, Karanjin, Lipoconjugated karanjin, Anticancer, Anti-inflammatory, Antimicrobial activity

Karanj (*Pongamia glabra*) seed contains a group of furanoflavonoids and the principal among them is karanjin[1]. Karanjin is well known to possess many potent biological activities as underlined in a recent review article[2]. Our own research showed excellent mosquito larvicidal activity of karanjin-rich crude extract from deoiled cake[3]. Several research groups carried out many structural modifications of karanjin to synthesize analogues and studied their biological activity performance. Most of these modification were made either by inclusion of heterocyclic moiety in the karanjin motif or by inclusion of substituent's on the phenyl ring or by attachment of bio-molecule[4-7]. Lipoconjugation of karanjin has not been reported earlier, which is going to be the focus of the present research work.

Flavonoids and furanoflavonoids are widely distributed in nature and plants containing such phytocomponents are often used in traditional system of medicines. Pharmacological studies of karanjin revealed diverse biological activities and many potential industrial applications[1]. In 2015, Guo *et al*.[8] reported moderate effect of karanjin on cell cycle arrest and induction of apoptosis in three cancer cell lines (A549, HepG2 and HL-60) in a dose and time dependent manner. Cancer chemopreventive role of pongapin and lanceolatin, other two known furanoflavones present in karanj seed was also reported in the literature[9]. Roy *et al*. studied the antitumour activity of karanjin and pongapin and found their chemopreventive potential in restricting the growth of cancer cell, more specifically the human cervical cancer cell line[10]. Protective role of karanjin in dimethylhydrazine-induced colon cancer in rats has also been documented in a very recent literature[11]. In this context, lipoconjugated karanjin was also evaluated for anticancer activity against different human cancer cell lines and compared with karanjin and demethylated karanjin. The objective is to find out increase or decrease in anticancer activity of karanjin due to lipoconjugation. Lipoconjugates were also evaluated for antimicrobial and antiinflammatory activities and compared with karanjin and demethylated karanjin. Both chain length and functional moiety present in the lipid chain was varied in order to study its effect on activity.

Experimental Details

All the chemicals used in this study were obtained from different commercial sources and were used without any further purification. Reactions were monitored on micro TLC with UV detection. Final purifications were carried out using silica gel (Rankem) 60-120 mesh. All ^{1}H and ^{13}C NMR spectra

were recorded on ADVANCE-300 and 400 (300 and 400 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR). Chemical shifts are reported in δ (ppm) with reference to TMS as internal standard. Molecular weights of unknown compounds were identified by ESI-MS and HR-MS (Electron Spray Ionization Technique). IR spectra were recorded in chloroform on a Perkin-Elmer FT-IR spectrum BX spectrometer.

Demethylation of Karanjin, 2

To a stirred solution of Karanjin (2 g, 1 mmol) in DCM (35 mL), Boron tribromide BBr_3 (0.3 mL, 20.54 mmol) was added slowly at 0°C. After completion of addition, the reaction mixture was stirred at 27°C and the progress of reaction was monitored by TLC. After 4 h, the reaction mixture was quenched with 20 mL of ice-cold water and the organic phase was separated. After evaporation of organic solvent under reduced pressure, water was added into the reaction mixture and the product was extracted with DCM and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography by eluting with ethyl acetate: hexane (30:70 v/v) which afforded the title compound in 80% yield (1.6 g, Light yellow colour solid). m.p.198-200°C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.60 (s, 1H, Ar-OH), 8.20-8.40 (m, 4H, Ar-H), 7.40-7.60 (m, 5H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.07, 155.54, 147.48, 144.81, 142.37, 137.50, 129.54, 127.66, 126.55, 125.59, 119.15, 114.94, 107.83, 102.46; IR ($CHCl_3$): 3386, 3019, 1215, 756 cm^{-1}; ESI-MS: *m/z* $[M+H]^+$ 279; HR-MS (ESI) *m/z* [M+H$^+$]: Calcd for $C_{17}H_{11}O_4$: 279.06519. Found: 279.06519 ($C_{17}H_{11}O_4$).

General procedure for the synthesis of Lipoconjugates

Lipid (1.0 mmol) was dissolved in 10 mL DCM followed by the addition of EDC.HCl (0.275, 1.43 mmol) and DMAP (0.175g, 1.43mmol) at 0°C. The reaction mixture was stirred for 10 min at the same temperature. After 10 min, demethylated karanjin (0.200 g, 1 mmol) was added to the stirred reaction mixture and stirred at 27°C. Progress of the reaction was monitored by TLC. After 16 h, the reaction mixture was quenched with aqueous NH_4Cl solution (20%) and the organic phase was separated from the aqueous phase. After evaporation of organic solvent under reduced pressure, water was added into the reaction mixture and the product was extracted with DCM and dried over anhyd. Na_2SO_4. The crude product was purified by column chromatography by eluting with ethyl acetate: hexane (30:70 v/v).

Spectral data of selected compounds

4-Oxo-2-phenyl-4*H*-furo[2,3-h]chromen-3-yl hexanoate, 3Ra: Isolated yield 75% (0.150 g, Light white solid), m.p.65-68°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19(d, 1H, *J* = 8.80 Hz, Ar-H), 7.92-7.89(m, 3H, Ar-H), 7.77(d, *J* = 2.20 Hz, 1H, Ar-H), 7.60-7.52(m, 3H, Ar-H), 7.17(d, *J* = 2.20 Hz, 1H, Ar-H), 2.17 (t, *J* = 7.32 Hz, 2H), 1.54 – 1.6 (m, 2H), 1.2 - 1.32 (m, 4H), 0.86 (t, *J* = 6.71 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.09, 170.92, 158.28, 155.50, 150.23, 145.85, 134.04, 131.11, 130.04, 128.64, 128.24, 119.05, 117.03, 110.32, 104.11, 33.89, 31.14, 24.45, 22.24, 13.84; IR ($CHCl_3$): 3019, 1215, 758 cm^{-1}; ESI-MS: *m/z* $[M+Na]^+$ 399; HR-MS (ESI) *m/z* [M+H$^+$]: Calcd for $C_{23}H_{21}O_5$: 377.13835. Found: 377.13835 ($C_{23}H_{21}O_5$).

4-Oxo-2-phenyl-4*H*-furo[2,3-h]chromen-3-yl octanoate, 3Rb: Isolated yield 80% (0.160 g, Light white solid). m.p.69-72°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19(d, 1H, *J* = 8.80 Hz, Ar-H), 7.92-7.89(m, 3H, Ar-H), 7.77(d, *J* = 2.20 Hz, 1H, Ar-H), 7.60-7.52(m, 3H, Ar-H), 7.17(d, *J* = 2.20 Hz, 1H, Ar-H), 2.44 – 2.50 (t, *J* =7.4Hz, 2H, CH_2), 1.69 – 1.78 (m, 2H, CH_2), 1.29 – 1.39 (m, 8H, $(CH_2)_4$, 0.79 – 0.90 (t, *J* = 6.7Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.19, 172.12, 170.93, 158.28, 155.51, 150.22, 145.85, 134.03, 131.10, 130.03, 128.24, 128.63, 119.03, 117.02, 110.33, 104.11, 33.93, 31.56, 28.96, 28.85, 24.75, 24.66, 22.54, 14.01; IR ($CHCl_3$): 3019, 1215, 766 cm^{-1}; ESI-MS: *m/z* $[M+Na]^+$ 427; HR-MS (ESI) *m/z* [M+H$^+$]: Calcd for $C_{25}H_{25}O_5$: 405.16739. Found: 405.16739 ($C_{25}H_{25}O_5$).

4-Oxo-2-phenyl-4*H*-furo[2,3-h]chromen-3-yl dodecanoate, 3Rc: Isolated yield 80% (0.160 g, Light white solid). m.p.73-76°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19(d, 1H, *J* = 8.80 Hz, Ar-H), 7.92-7.89(m, 3H, Ar-H), 7.77(d, *J* = 2.20 Hz, 1H, Ar-H), 7.60-7.52(m, 3H, Ar-H), 7.17(d, *J* = 2.20 Hz, 1H, Ar-H),δ 2.44 – 2.50 (t, *J* =7.4Hz, 2H, CH_2), 1.69 – 1.78 (m, 2H, CH_2), 1.29 – 1.39 (m, 16H, $(CH_2)_8$, 0.82 – 0.91 (t, *J* = 6.7Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): 179.56, 172.15, 170.96, 158.32, 155.55, 150.27, 145.85, 134.06, 131.12, 130.06, 128.65, 128.28, 119.08, 117.06, 110.36, 104.14, 33.98, 31.88, 29.58, 29.03, 29.40, 29.21, 29.29, 24.79, 24.67, 22.65, 14.08; IR ($CHCl_3$): 3020, 1215, 756 cm^{-1}; ESI-MS *m/z* $[M+Na]^+$ 483; HR-MS (ESI) *m/z* [M+H$^+$]: Calcd for $C_{29}H_{33}O_5$: 461.22852. Found: 461.22852 ($C_{29}H_{33}O_5$).

4-Oxo-2-phenyl-4*H*-furo[2,3-h]chromen-3-yl undec-10-enoate, 3Rd: Isolated yield 70% (0.140 g, yellow solid). m.p.59-64°C. ^{1}H NMR (300 MHz,

$CDCl_3$): δ 8.19(d, 1H, *J* = 8.80 Hz, Ar-H), 7.92-7.89(m, 3H, Ar-H), 7.77(d, *J* = 2.20 Hz, 1H, Ar-H), 7.60-7.52(m, 3H, Ar-H), 7.17(d, *J* = 2.20 Hz, 1H, Ar-H), 5.82 (m, 1H, =CH), 4.83 – 4.94 (m, 2H, $=CH_2$), 3.08 (dd, *J* = 5.66, 13.97 Hz, 1H), 2.98 (dd, *J* = 6.04, 13.97 Hz, 1H), 2.17 (t, *J* = 7.36 Hz, 2H), 1.57 (m, 2H), 1.25 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.14, 170.93, 158.31, 155.55, 150.25, 145.86, 139.12, 131.11, 130.05, 128.65, 128.26, 134.04, 119.06, 117.05, 114.09, 110.36, 104.13, 33.94, 33.74, 29.20, 29.14, 28.99, 28.85, 24.76, 24.64; IR ($CHCl_3$): 3019, 1215, 770 cm^{-1}; ESI-MS: *m/z* $[M+Na]^+$ 467; HR-MS (ESI) *m/z* $[M+H^+]$: Calcd for $C_{28}H_{29}O_5$: 445.19739. Found: 445.19739 ($C_{28}H_{29}O_5$).

4-Oxo-2-phenyl-4*H*-furo[2,3-h]chromen-3-yl octadec-9-enoate, 3Re: Isolated yield 60% (0.120 g, light pink semi solid). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (d, 1H, *J* = 8.80 Hz, Ar-H), 7.92-7.89 (m, 3H, Ar-H), 7.77 (d, *J* = 2.20 Hz, 1H, Ar-H), 7.60-7.52 (m, 3H, Ar-H), 7.17 (d, *J* = 2.20 Hz, 1H, Ar-H), 5.32 – 5.36 (m, 2H, = CH_2), 2.47 – 2.52 (t, *J* =7.4Hz, 2H, CH_2), 1.95 – 2.11 (m, 5H, $(=CH\text{-}CH)_2$, 1.25 – 1.43 (m, 20H, $(CH_2)_{10}$), 0.80 – 0.89 (t, *J* = 6.7Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.13, 170.92, 158.32, 155.55, 150.27, 145.85, 131.12, 134.06, 129.97, 129.68, 128.65, 128.28, 122.07, 119.08, 117.06, 110.37, 104.15, 33.94, 31.87, 30.87, 29.73, 29.65, 29.49, 29.28, 29.01, 27.18, 24.66, 24.78, 22.65, 29.11, 14.08; IR ($CHCl_3$): 3450, 3019, 1215, 757 cm^{-1}; ESI-MS: *m/z* $[M+Na]^+$ 565; HR-MS (ESI) *m/z* $[M+H^+]$: Calcd for $C_{35}H_{43}O_5$: 543.31050. Found: 543.31050 ($C_{35}H_{43}O_5$).

4-Oxo-2-phenyl-4*H*-furo[2,3-h]chromen-3-yl 5-(1,2-dithiolan-3-yl) pentanoate, 3Rf: Isolated yield 70% (0.140 g, yellow solid). m.p.138-146°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19(d, 1H, *J* = 8.80 Hz, Ar-H), 7.92-7.89(m, 3H, Ar-H), 7.77(d, *J* = 2.20 Hz, 1H, Ar-H), 7.60-7.52(m, 3H, Ar-H), 7.17(d, *J* = 2.20 Hz, 1H, Ar-H), 3.75 (s, 3H), 3.48 – 3.55 (m, 1H), 3.07 – 3.19 (m, 3H), 2.93 – 2.99 (m, 1H), 2.4 – 2.46 (m, 1H), 2.13 – 2.23 (m, 2H), 1.84 – 1.91 (m, 2H), 1.55 – 1.68 (m, 4H), 1.3 – 1.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.02, 170.61, 158.32, 155.54, 150.25, 145.89, 134.01, 131.19, 130.01, 128.71, 128.25, 127.46, 119.06, 117.07, 110.39, 104.15, 56.20, 40.15, 38.45, 34.53, 33.70, 30.88, 28.56, 24.52; IR ($CHCl_3$): 3020, 1215, 756 cm^{-1}; ESI-MS: *m/z* $[M+Na]^+$ 489; HR-MS (ESI) *m/z* $[M+H^+]$: Calcd for $C_{25}H_{23}O_5S_2$: 467.09509. Found: 467.09509 ($C_{25}H_{23}O_5S_2$).

Antimicrobial activity

Anti-bacterial activity

The minimum inhibitory concentrations (MIC) of newly synthesized compounds were tested against three representative Gram-positive organisms *viz*. *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 96), *Staphylococcus epidermidis* and Gram-negative organisms *viz*. *Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 741), and *Klebsiella pneumoniae* (MTCC 618) by Microdilution method as recommended by CLSI Standard Protocol[16]. The lowest concentration at which inhibition of the microbial growth observed was considered the MIC (µg/mL) value for the tested compound. Penicillin and Streptomycin were used as standard drugs.

Anti-fungal activity

In vitro antifungal activity of the newly synthesized compounds was studied against the fungal strains, *Candida albicans* (MTCC 227), *Candida rugosa* (NCIM 3467) and *Saccharomyces cervisiae* (MTCC 36) of yeasts and *Aspergillus flavus* (MTCC 277), and *Aspergillus niger* (MTCC 282), by Agar Well Diffusion Method[17]. Results are expressed as diameters of the zones of inhibition measured in millimetre. Amphotericin-B was used as positive control.

***In vitro* cytotoxicity cssay**

All the synthesized compounds were screened for *in vitro* cytotoxicity on a panel of five different cancer cell lines such as such as DU 145: Human Prostate cancer (ATCC® HTB81™), MDAMB231: Human Breast cancer (ATCC® HTB26™), HeLa: *Homo sapiens* cervix adenocarcinoma (ATCC® CCL-2.1™); HepG2: liver hepatocellular carcinoma (ATCC® HB-8065™); SK-OV-3: Human Ovarian cancer (ATCC® HTB 77™) cell lines were obtained from the American Type Culture Collection, Manassas, VA, USA. The cytotoxicity was determined using MTT assay following our earlier published work[18]. The effects of the different synthesized compounds on the viability of the cancer cell lines were measured at 540 nm using a multimode reader (Infinite® M200, Tecan, Switzerland). The IC_{50} values (50% inhibitory concentration) were calculated from the plotted absorbance data of the dose–response curves. The assay was performed using doxorubicin as positive controls and 1% DMSO as a vehicle control. In order to account for the toxicity of DMSO, the values obtained for the DMSO control were

subtracted from those of the test compounds. The IC_{50} values (in mM) are expressed as the average of two independent experiments.

***In vivo* anti-inflammatory activity - Carrageenan induced rat paw edema**

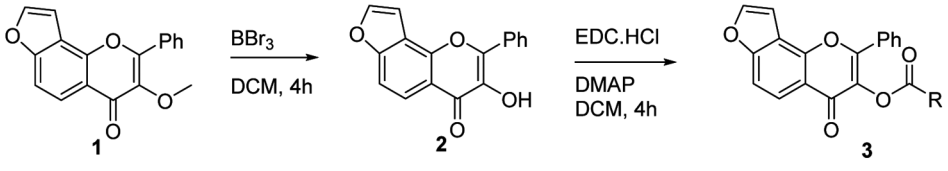
Male Albino Wistar rats weighing between 130-150 g were used for the experiments. They were kept in polypropylene cages under standard laboratory conditions (12: 12 hr light/dark cycle at 24°C). Rats were provided with commercial rat diet (NIN, Hyderabad) and water *adlibitum*. The experiments were conducted after obtaining approval from Institutional Animal Ethical Committee of Indian Institute of Chemical Technology (IICT/03/2016). Animals were quarantined and acclimatized to laboratory conditions for 7 days prior to study initiation. Animals were observed for general health and suitability for testing during this period.

The anti-inflammatory activity of the test compounds was evaluated in Wistar rats by employing the method of Winter *et al*.[15] Animals were fasted overnight and were divided them into control, standard and different test groups. The test compounds were administered by oral route as gum acacia suspension (2% w/v) at the dose of 100 mg/kg, Animals in the standard group received Indometacin at the dose of 10 mg/kg, by oral route. Rats in the control group received the vehicle solution without test compounds. One hour after test drugs administration, rats in all the groups were challenged with 0.1 mL of 1% carrageenan in the sub plantar region of right hind paw. Paw volumes were measured before and after 3 h after the challenge of carrageenan using digital plethysmometer (Ugo Basile, Italy). The percent inhibition of paw volume for treated groups was calculated by comparing with mean paw volume of control group.

Results and Discussion

During expelling of karanj seed for the extraction of oil, karanjin gets distributed between the expelled cake and the extracted oil. A scalable process was developed in our laboratory for the extraction of karanjin (97% purity) from the expelled cake[12]. Isolated karanjin was further purified by column chromatography and the final pure karanjin was used as starting material for the synthesis of six lipoconjugates as per Scheme 1. Synthesis commenced with demethylation of Karanjin (**1**) under stirred condition in presence of BBr_3 to give aromatic alcohol (**2**). After column purification (isolated yield 80%) and structural characterization of demethylated karanjin (**2**), the hydroxyl functionality was esterified with a series of carboxylic acids, namely aliphatic saturated (caprylic, capric and lauric acids), unsaturated (10-undecenoic and oleic acid) and 1,2-dithiolane containing carboxylic acids (lipoic acid) in presence of EDC as coupling reagent to get the six acylated analogues of karanjin **3(Ra-Rf)** in very good yields (60-80% isolated yield). All compounds were well characterized using mass, IR, ^1H and ^{13}C NMR.

All synthesized compounds along with karanjin were tested for their antimicrobial, anticancer and anti-inflammatory activities. Lipoconjugation does not seem to improve the antibacterial activity of karanjin against studied Gram-positive (*Bacillus subtilis*, *Staphylococcus aureus* and *Staphylococcus epidermidis*) and Gram-negative organisms (*Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*). Even the studied compounds did not show any antifungal activity against some selected fungal strains (*Candida albicans*, *Candida rugosa*, *Saccharomyces cervisiae*, *Aspergillus flavus* and *Aspergillus niger*). Anticancer activity was studied against different human cancer cell lines such as prostate (DU145), breast (MDAMB-231), cervical (HeLa), liver (HepG2) and ovarian (SK-OV-3) and results are given in Table 1. None of the studied compounds show any inhibitory activity against the growth of liver (HepG2) and ovarian (SK-OV-3) cancer cell lines. Against the growth of cervical cancer line (HeLa), only shortest chain lipoconjugates Lp-



3Ra: Caproic acid; **3Rb:** Caprylic acid
3Rc: Lauric acid; **3Rd:** 10-Undecenoic acid
3Re: Oleic acid **3Rf:** Lipoic acid

Scheme 1 — Synthesis of acylated derivative of karanjin

Table 1 — Anticancer activity of karanjin (Kar), demethylated karanjin (DM-Kar) and six synthesized karanjin lipo-conjugates on different human cancer cell lines

Test Compd	IC50 values (μM)				
	DU145	MDAMB231	HeLa	HepG2	SK-OV-3
Kar (**1**)	24.4 ± 0.66	16.5 ± 0.39	59.9 ± 0.76	NA	NA
DM-Kar (**2**)	68.6 ± 0.84	24.3 ± 0.55	156.4 ± 0.97	NA	NA
Lp-Cap-Kar (**Ra**)	7.9 ± 0.42	46.1 ± 0.91	63.3 ± 0.78	NA	NA
Lp-Cpy-Kar (**Rb**)	47.3 ± 0.85	25.1 ± 0.61	NA	NA	NA
Lp-Lar-Kar (**Rc**)	–	–	–	–	–
Lp-UDA-Kar (**Rd**)	25.5 ± 0.65	33.2 ± 0.87	NA	NA	NA
Lp-Oleic-Kar (**Re**)	41 ± 0.71	21.5 ± 0.68	NA	NA	NA
Lp-Lip-Kar (**Rf**)	54.6 ± 0.69	23.5 ± 0.88	NA	NA	NA
Doxorubicin	0.8 ± 0.12	0.7 ± 0.11	0.8 ± 0.13	0.7 ± 0.14	0.7 ± 0.12

Table 2 — Anti-inflammatory activity of synthetic compounds by Carrageenan induced model in Wistar rats

Test Compd[@]	Paw Volume			Anti-inflammatory activity (%)
	Initial	Final	Difference	
Control	1.13 ± 0.03	2.53 ± 0.03	1.40 ± 0.01	-
Kar (**1**)	1.14 ± 0.03	2.32 ± 0.03	1.18 ± 0.01	15.23 ± 3.17
DM-Kar (**2**)	1.10 ± 0.03	2.41 ± 0.03	1.31 ± 0.01	5.89 ± 3.17
Lp-Oleic-Kar (3**Re**)	1.18 ± 0.02	2.55 ± 0.04	1.36 ± 0.02	3.57 ± 2.14
Lp-Lip-Kar (**3Rf**)	1.18 ± 0.02	2.35 ± 0.04	1.17 ± 0.04	16.19 ± 2.14
Indomethacin	1.20 ± 0.04	1.90 ± 0.08	0.70 ± 0.04	49.76 ± 3.50

Values are Mean ± S.E.M; [@] No activity for compounds **3Ra**, **3Rb**, **3Rc**, **3Rd**

Cap-Kar (**3a**) showed activity similar to karanjin (**1**). In prostate cancer cells (DU145), the lipoconjugate Lp-Cap-Kar (**3a**) showed inhibition at lowest concentration (IC50 = 7.9 ± 0.42 μM), depicting improvement in activity due to lipoconjugation. In Breast cancer cells (MDAMB-231), karanjin (**1**) showed inhibition at relatively low concentration (IC50 = 16.5 ± 0.39 μM) compared to other studied compounds having activity in the range of 22 to 46 μM. An interesting observation is impressive growth inhibitory activity of Lp-Cap-Kar (**3a**) on prostate cancer cells but does not show up significant activity in breast cancer cells indicating cancer cell specificity and potency. Overall, lipoconjugation does not have profound effect on the anticancer activity of karanjin against any studied cancer cell lines except the shorter chain analogue (**3a**) showing improvement against prostate cancer cell line.

Polar extracts of root and seed of karanj tree are reported to possess anti-ulcerogenic activity against acute gastric ulcer[13]. This anti-inflammatory response has been linked to two furanoflavones, pongapin and karanjin[14]. As part of the present research, it was planned to carry out anti-inflammatory activity of the lipoconjugates along with karanjin and demethylated karanjin in Carrageenan induced rat model employing the method of Winter *et al*.[15] Results obtained are shown in Table 2, depicting no improvement in antiinflammatory activity of karanjin due to lipoconjugation except mild increase in case of Lp-Lip-Kar (**3f**).

Conclusion

In conclusion, six lipoconjugates of karanjin were synthesized following a two step reactions - demethylation of karanjin by the treatment of BBr_3 in the first step and the resultant aromatic alcohol was esterified with six different acids in the second step. The prime objective was to find the effect of lipoconjugation of karanjin on its bioactivities. Results obtained indicated Moderate impact of lipoconjugation on the bioactivity of karanjin especially on its anticancer and anti-inflammatory activities except the shorter chain lipoconjugate (**3Ra**) showing improvement in anticancer activity against prostate cancer cell line.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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