Indian Journal of Chemistry
Vol. 46B, September 2007, pp. 1459-1465

Papers

A facile microwave assisted synthesis and antimicrobial activities of naturally occurring (*E*)-cinnamyl (*E*)-cinnamates and (*E*)-aryl cinnamates

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Received 27 June 2006; accepted (revised) 5 April 2007

Benzaldehydes **1a-e** on reaction with phosphorane **3** and aldehydes **2a-e** with phosphorane **4** under microwave irradiation provide the (*E*)-cinnamyl (*E*)-cinnamates **5a-e** and (*E*)-aryl cinnamates **6a-e** respectively in high yield. Cinnamates **5a-e** and **6a-e** exhibit antibacterial and antifungal activity.

Keywords: Microwave irradiation, cinnamyl cinnamates, aryl cinnamates, Wittig reaction, antibacterial activity, antifungal activity, inhibition zone

The cinnamyl cinnamates **5a-d** have been isolated from various natural sources[1] including propolis[2–4]. Propolis or bee glue, a natural resinous hive product gathered by honeybees from buds and exudates of certain trees and plants, has been considered as a protective barrier against their enemies. The honeybees use propolis mixed with bee's wax for general sealing purpose and as a coolant. Propolis has been used as a folk medicine in many regions of the world. Propolis has been reported to possess various biological activities such as antiviral[5], antibacterial[6], fungicidal[7], antiinflammatory[8] and anticancer[9].

Cinnamyl cinnamate **5d** isolated from the essential oil *Lavuango scandens*[10] is of high medicinal value especially in curing baldness. (*E*)-cinnamyl-(*E*)-cinnamate **5d** has also been used[11] in industry for the manufacturing of soaps, detergents, lotions and perfumes.

An aryl cinnamate, difengpin **6a**, has been isolated[12] from *Illicium difengpi*. In Chinese pharmacopaeia the dried bark of *Illicium difengpi* is used as antirheumatic drug for relieving lumbago and pain in the knees[12].

Aryl cinnamates are reported to possess anticancer[13], antiinflammatory[13], antifungal[14] and antialopecic[15] activity. Aryl cinnamates have been used for the synthesis of aziridins[16], 2-substituted biphenyls[17], flavanones[18], cinnamoyl coumaranones[19], 2-styryl chromones[20], styryl pyrazoles[21], stilbenes[21], β-truxinic acid[22], coumarins[23] and substituted benzofuranones[24]. Aryl cinnamates are also used for the synthesis of duocarmycin[25] and DC-89 derivatives[26] which show strong antitumour, neoplasm inhibitory and antibacterial activity.

Methods involving microwave irradiation[27] have been frequently used in synthetic organic chemistry, as these methods are efficient and provide the final products in high yield and in short time. Herein is reported a convenient, general and high yield single step method for the synthesis of cinnamyl cinnamates **5a-e** and aryl cinnamates **6a-e** from easily available benzaldehydes **1a-e** and **2a-e** as shown in (**Schemes I** and **II)** respectively. Benzaldehyde **1a-e** on reaction with phosphorane **3** (Ref. 28) under microwave irradiation for 2-3 min provided the (*E*)-cinnamyl-(*E*)-cinnamate **5a-e** in 71-91% yield. When benzaldehydes **2a-e** were reacted with phosphorane **4** (Ref. 29) under microwave irradiation for 2 min the (*E*)-aryl cinnamates **6a-e** were obtained in 73-86% yield.

In conclusion, a stereoselective, general method has been developed for the synthesis of (*E*)-cinnamyl-(*E*)-cinnamate **5a-e** and (*E*)-aryl cinnamates **6a-e** using Wittig reaction under microwave irradiation. The products are obtained under mild conditions and in very short time. The present method is highly efficient and provides the title compounds in excellent yields.

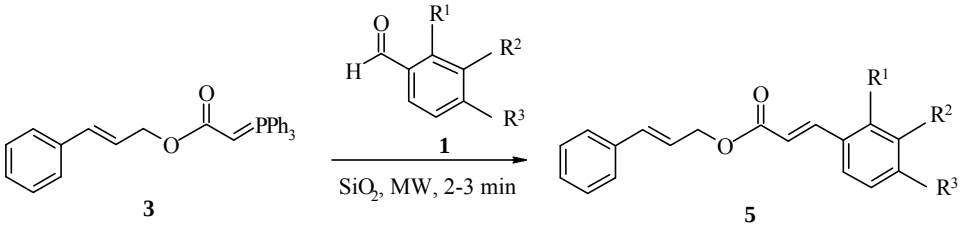
Experimental Section

All melting points are uncorrected. IR spectra were recorded on Shimadzu FTIR-8400S spectrometer using KBr pellets and in chloroform. ^{1}H NMR spectra were recorded on Varian Mercury spectrometer at 300

MHz and AC 200 Bruker spectrometer at 200 MHz in $CDCl_3$ using TMS as an internal standard. Elemental analysis was obtained using Perkin-Elmer carbon-hydrogen analyzer. Kenstar-OM 9918C, 2450 MHz (900 W) microwave oven was used for microwave irradiation. Silica gel 60-120 mesh supplied by S.D. Fine-Chem Ltd. (India) was activated by irradiation for 10 min before use. Homogeneity of the compounds was checked by TLC.

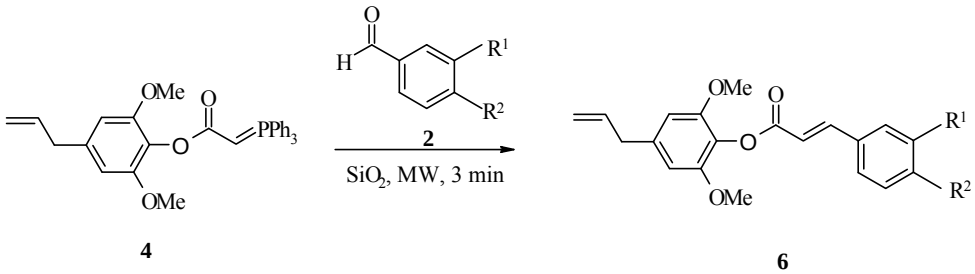
General procedure for the synthesis of cinnamyl cinnamates 5a-e. Silica gel (3.0 g) was added to a solution of benzaldehyde **1a-e** (1 mmol) and phosphorane **3** (1.2 mmol) in dichloromethane (5 mL) and the reaction mixture was stirred for 2 min. The solvent was removed and the residual powder was dried *in vacuo*. It was spread on a petri dish and irradiated in microwave oven for 2-3 min (monitored by TLC). After completion of the reaction it was chromatographed over silica gel using hexane:ethyl acetate (9:1) as an eluent to afford **5a-e**.

(*E*)-Cinnamyl-(*E*)-isoferulate 5a. Irradiated for 3 min. White solid. Yield 0.24 g, 77%; m.p. 69°C, (Lit.[28] 69-70°C); IR (KBr): 1686, 1603, cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.92 (3H, s, OCH_3), 4.86 (2H, d, J = 5.9 Hz, $-CH_2O-$), 5.68 (1H, s, -OH, exchangeable with D_2O), 6.29-6.37 (2H, m, H-8 and H-8′), 6.71 (1H, d, J = 15.8 Hz, H-7′), 6.84 (1H, d, J = 8.2 Hz, H-5), 7.05 (1H, bd, J = 8.2 Hz, H-6), 7.15 (1H, s, H-2), 7.25-7.42 (5H, m, Ar-H), 7.68 (1H, d, J = 16.4 Hz, H-7). Anal. Found: C, 73.23; H, 5.65. Calcd. for $C_{19}H_{18}O_4$: C, 73.54; H, 5.80%.



1, 5	R 1	R 2	R 3
a	H	OH	OMe
b	H	OMe	OH
c	H	OMe	OMe
d	H	H	H
e	OMe	H	OMe

Scheme I



2, 6	R 1	R 2
a	H	H
b	OMe	OH
c	OH	OMe
d	OMe	OMe
e	-OCH2O-	

Scheme II

(*E*)-Cinnamyl-(*E*)-ferulate 5b. Irradiated for 3 min. Viscous liquid. Yield 0.22 g, 72%; (Lit.[28] Viscous liquid); IR ($CHCl_3$): 1691, 1635, 1597, 1155 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.0 (3H, s, OCH_3), 4.89 (2H, d, *J* = 7.0 Hz, -CH_2O-), 6.0 (1H, bs, -OH, exchangeable with D_2O), 6.34-6.44 (2H, m, H-8 and H-8′), 6.74 (1H, d, *J* = 16.9 Hz, H-7′), 6.94 (1H, d, *J* = 8.5 Hz, H-5), 7.08 (1H, d, *J* = 8.5, H-6), 7.14 (1H, bd, H-2), 7.29-7.47 (5H, m, Ar-H), 7.7 (1H, d, *J* = 16.9 Hz, H-7). Anal. Found: C, 73.74; H, 5.97. Calcd. for $C_{19}H_{18}O_4$: C, 73.54; H, 5.80%.

(*E*)-Cinnamyl-(*E*)-*O*,*O*-dimethyl caffeate 5c. Irradiated for 2 min. White solid. Yield 0.28 g, 86%; m.p. 99-100°C (Lit.[28] 99-101°C); IR (KBr): 1707, 1625, 1600, 1161 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.94 (6H, s, 2 × OCH_3), 4.90 (2H, d, *J* = 6.6 Hz, –CH_2O–), 6.40 (2H, m, H-8 and H-8′), 6.74 (1H, d, *J* = 16.9 Hz, H-7′), 6.90 (1H, d, *J* = 8.9 Hz, H-5), 7.02 (1H, bd, H-2), 7.15 (1H, d, *J* = 8.9 Hz, H-6), 7.30-7.46 (5H, m, Ar-H), 7.71 (1H, d, *J* = 16.9 Hz, H-7). Anal. Found: C, 73.75; H, 6.01. Calcd. for $C_{20}H_{20}O_4$: C, 74.07; H, 6.17%.

(*E*)-Cinnamyl-(*E*)-cinnamate 5d. Irradiated for 2 min. White solid. Yield 0.24 g, 91%; m. p. 40-42°C, (Lit.[30] 40-41°C); IR (KBr): 1711, 1635, 1530, 1215 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.92 (2H, d, *J* = 6.6 Hz, –CH_2O–), 6.4 (1H, dt, *J* = 16.6 and 6.6 Hz, H-8′), 6.52 (1H, d, *J* = 16.6 Hz, H-8), 6.76 (1H, d, *J* = 16.6, H-7′), 7.37-7.60 (10H, m, Ar-H), 7.70 (1H, d, *J* = 16.6 Hz, H-7). Anal. Found: C, 82.08; H, 6.30 Calcd. for $C_{18}H_{16}O_2$: C, 81.81; H, 6.06%.

(*E*)-Cinnamyl-(*E*)-2,4-dimethoxy cinnamate 5e. Irradiated for 3 min. Viscous liquid. Yield 0.27 g, 83%; IR ($CHCl_3$): 1701, 1604, 1161 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.88 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 4.90 (2H, d, *J* = 6.8 Hz, –CH_2O–), 6.46 (1H, d, *J* = 2.2 Hz, H-3), 6.51 (1H, dd, *J* = 8.5 and 2.2 Hz, H-5), 6.52-6.56 (2H, m, H-8 and H-8′), 6.74 (1H, d, *J* = 15.9 Hz, H-7′), 7.30-7.45 (5H, m, Ar-H), 7.49 (1H, d, *J* =8.5 Hz, H-6), 7.6 (1H, d, *J* = 15.9 Hz, H-7). Anal. Found: C, 73.76; H, 6.02. Calcd. for $C_{20}H_{20}O_4$: C, 74.07; H, 6.17%.

General procedure for the synthesis of aryl cinnamates 6a-e. Silica gel (3.0 g) was added to a solution of appropriate aldehyde **2a-e** (0.83 mmol) and phosphorane **4** (0.49 g, 1 mmol) in dichloromethane (5 mL), and the reaction mixture was stirred for 2 min. The solvent was removed, and the residual powder was dried *in vacuo*. It was spread in a petri dish, irradiated in a microwave oven for 3 min and chromatographed over silica gel using hexane:ethyl acetate (9:1) as an eluent to afford aryl cinnamates **6a-e** as white solids. All these esters were purified by recrystallization from ethyl acetate-hexane.

4-Allyl-2,6-dimethoxyphenylcinnamate (Difengpin) 6a. Yield 0.22 g, 82%; m.p. 153-55°C (Lit.[12b] 153-55°C); IR (KBr) 1737 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.39 (2H, d, *J* = 6 Hz, CH_2=CH–CH_2), 3.82 (6H, s, 2×OCH_3), 5.09-5.19(2H, m, CH_2=CH–CH_2–), 5.91-6.05 (1H, m, CH_2=C*H*-CH_2), 6.48 (2H, s, H-3, H-5), 6.73 (1H, d, *J* =16 Hz, H-8′), 7.35-7.45 (3H, m, Ar-H), 7.55-7.65 (2H, m, Ar-H), 7.89 (1H, d, *J* = 16 Hz, H-7′). Anal. Found: C, 73.77; H, 6.02. Calcd. for $C_{20}H_{20}O_4$: C, 74.07; H, 6.17%.

4-Allyl-2,6-dimethoxyphenyl ferulate 6b. Yield 0.26 g, 85%; m.p. 159-61°C (Lit.[29] 159-61°C); IR (KBr) 1728 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.38 (2H, d, *J*=6 Hz, CH_2=CH–CH_2), 3.82 (6H, s, 2 × OCH_3), 3.93 (3H, s, OCH_3), 5.10-5.19 (2H, m, CH_2=CH–CH_2), 5.89 (1H, s, -OH, exchangeable with D_2O), 5.95-6.10 (1H, m, CH_2=C*H*-CH_2), 6.47 (2H, s, H-3, H-5), 6.58 (1H, d, *J* = 16 Hz, H-8′), 6.92 (1H, d, *J* = 8 Hz, H-5′) 7.11 (1H, dd, *J* = 8 Hz and 2 = Hz, H-6′), 7.26 (1H, d, *J* = 2 Hz, H-2′), 7.81 (1H, d, *J* = 16 Hz, H-7′). Anal. Found: C, 67.75; H, 5.71. Calcd. for $C_{21}H_{22}O_6$: C, 68.10; H, 5.94%.

4-Allyl-2,6-dimethoxyphenylisoferulate 6c. Yield 0.25 g, 82%; m.p. 139-41°C (Lit.[29] 139-41°C); IR (KBr) 1736 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.38 (2H, d, *J* =8 Hz, CH_2=CH–CH_2), 3.82 (6H, s, 2 × OCH_3), 3.94 (3H, s, OCH_3), 5.09-5.19 (2H, m, CH_2=CH–CH_2–), 5.65 (1H, s, OH, exchangeable with D_2O), 5.91-6.0 (1H, m, CH_2=C*H*-CH_2), 6.47 (2H, s, H-3, H-5), 6.57 (1H, d, *J* = 16 Hz, H-8′), 6.86 (1H, d, *J* = 8 Hz, H-5′) 7.09 (1H, dd, *J* = 8 and 2 Hz , H-6′), 7.19 (1H, d, *J* = 2 Hz, H-2′), 7.79 (1H, d, *J* = 16 Hz, H-7′). Anal. Found: C, 68.40; H, 5.77. Calcd. for $C_{21}H_{22}O_6$: C, 68.10; H, 5.94%.

4-Allyl-2, 6-dimethoxyphenyl-3, 4-dimethoxycinnamate 6d. Yield 0.23 g, 73%; m.p. 131-32°C (Lit.[29] 131-32°C); IR (KBr) 1720 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.39 (2H, d, *J* = 6 Hz, CH_2=CH–CH_2), 3.82 (6H, s, 2 × OCH_3), 3.93 (6H, s, 2 × OCH_3), 5.10-5.18 (2H, m, CH_2=CH–CH_2–), 5.9-6.1 (1H, m, CH_2=C*H*-CH_2), 6.48 (2H, s, H-3, H-5), 6.6 (1H, d, *J* = 16 Hz, H-8′), 6.89 (1H, d, *J* = 8.1 Hz, H-5′), 7.18 (1H, dd, *J* = 8 and 2 Hz, H-6′); 7.27 (1H, d, *J* = 2 Hz, H-2′), 7.83 (1H, d, *J* = 16 Hz, H-7′). Anal. Found: C, 68.57; H, 6.05. Calcd. for $C_{22}H_{24}O_6$: C, 68.75; H, 6.25%.

4-Allyl-2,6-dimethoxyphenyl-3,4-methylenedioxy-cinnamate 6e. Yield 0.25 g, 86%; m.p. 122-24°C (Lit.[29] 122-24°C); IR (KBr):1724 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.38 (2H, d, J = 6.6 Hz, CH_2=CH–CH_2), 3.83 (6H, s, 2 × OCH_3), 5.01-5.18 (2H, m, CH_2=CH–CH_2–), 5.9-6.01 (3H, m, CH_2=CH–CH_2 and –O–CH_2–O–), 6.48 (2H, s, H-3, H-5), 6.61 (1H, d, J = 16.2 Hz, H-8′), 6.85 (1H, d, J = 7.5 Hz, H-5′) 7.04-7.1 (2H, m, Ar-H); 7.83 (1H, d, J = 16.2 Hz, H-7′). Anal. Found: C, 68.20; H, 5.22. Calcd. for $C_{21}H_{20}O_6$: C, 68.47; H, 5.43%.

Bioassay

Bioassay is an important and crucial factor in evaluation of bioactivity of the compounds and is helpful in establishing the structure-activity relationship (SAR). Cinnamyl cinnamates **5a-e** and aryl cinnamates **6a-e** have been tested for their antimicrobial potency such as antibacterial and antifungal activity against different human pathogenic bacteria and fungi, respectively.

Antibacterial activity of cinnamyl cinnamates 5a-e. The antibacterial activity of cinnamyl cinnamates **5a** and **5d** was studied at a concentration of 100 μg/disc against five bacterial species, *viz*, *Staphylococcus aureus, Escherichia coli, Salmonella typhi, Shigella dysenteriae* and *Shigella soneii.* For the detection of antibacterial activity, the filter paper disc (6 mm disc) diffusion method[31] was used. Gentamycin (20 μg/disc) was used as standard antibacterial agent. Nutrient agar (NA) was used as basal medium for test bacteria. These agar media were inoculated with 0.5 mL of the 24 hr liquid cultures containing 10^7 microorganisms/mL. The diffusion time was 1 hr at 5°C and incubation time was 24 hr at 37°C for bacteria. Disc with only DMSO was used as control. Inhibitory activity was measured as the inhibition zones (diameter, mm). The results are depicted in **Table I**.

The same study was carried out with other three cinnamyl cinnamates **5b, 5c** and **5e** against ten test bacterial species, *viz*, *Salmonella typhi, Salmonella paratyphi A, Salmonella paratyphi B, Shigella soneii, Shigella flexnari, Pseudomonas aeruginosa, Bacillus subtilis, Proteus vulgaris, Staphylococcus aureus* and *Escherichia coli*. Ampicilin (20 μg/disc) was used as standard antibacterial agent. The results are summarized in **Table II**.

Antifungal activity of cinnamyl cinnamates 5a-e. The antifungal activity of cinnamyl cinnamates **5a** and **5d** were studied at a concentration of 100 μg/disc against two fungi, *viz*, *Asperigillus niger* and *Candida albicans*. For the detection of antifungal activity, the filter paper disc (6 mm disc) diffusion method was used. Amphotericin (20 μg/disc) was used as standard antifungal agent. Nutrient agar (NA) was used as basal medium for test fungi. These agar media were inoculated with 0.5 mL of the 24 hr liquid cultures containing 10^7 microorganisms/mL. The diffusion time was 1 hr at 5°C and the incubation time was 7 days at 30°C for fungi. Disc with only DMSO was used as control. Inhibitory activity was measured as the inhibition zones (diameter, mm). Both compounds were found to be totally inactive against these fungal species.

Similarly antifungal activity of other three cinnamyl cinnamates **5b, 5c** and **5e** was evaluated against the same test fungi species using a different standard antifungal agent, Griseofulvin (20 μg/disc). The results are depicted in **Table III**.

Antibacterial activity of aryl cinnamtes 6a-e. The antibacterial activity of aryl cinnamates **6a-e** was studied at a concentration (100 μg/disc) against ten bacteria, *viz*, *Salmonella typhi, Salmonella paratyphi A, Salmonella paratyphi B, Shigella soneii, Shigella flexneri*, *Pseudomonas aeruginosa, Bacillus subtilis, Proteus vulgaris, Staphylococcus aureus* and

Table I — Antibacterial screening for cinnamyl cinnamates **(5a** and **5d)**

Test Microorganisms Bacteria	**5a**	**5d**	Standard drug Gentamycin
S. aureus	12±2	10±2	17±1
E. coli	9±1	8±1	18±1
S. typhi	16±1.5	10±1.5	18±1
S. dysenteriae	9±0.5	10±0.5	18±1
S. soneii	11±1	12±1	17±1

Table II — Antibacterial screening for cinnamyl cinnamates **(5b, 5c** and **5e)**

Test Microorganisms Bacteria	**5b**	**5c**	**5e**	Standard drug Ampicillin
S. typhi	-----	12.1±1.2	12.2±2	14.5±1
S. paratyphae A	11.2±1	-----	-----	15.3±1
S. paratyphae B	-----	10.2±0.8	10.4±1	13.6±1
S. sonnei	12.2±0.5	11.8±1.2	10.8±0.5	16.3±1
S. flexneri	13.1±0.8	11.7±1.5	11.7±0.8	11.7±0.8
P. aeruginosa	12.2±0.5	---	12.3±1	19.5±1
B. subtilis	10.7±1	12.1±1	-----	5.6±1
P. vulgaris	12.2±0.6	14.2±0.5	11.6±0.6	18.7±1

Table III — Antifungal screening for cinnamyl cinnamates (**5b, 5c** and **5e**)

Test Microorganisms Fungi	**5b**	**5c**	**5e**	Standard drug Griseofulvin
A. niger	—	12.3±0.5	12.3±0.8	14.3±1
C. albicans	10.6±1	—	11.2±0.5	16.1±1

Escherichia coli. For the detection of antibacterial activities, the filter paper disc (6 mm disc) diffusion method was used. Ampicilin (100 μg/disc) was used as standard antibacterial agent. Nutrient agar (NA) was used as basal medium for test bacteria. These agar media were inoculated with 0.5 mL of the 24 hr liquid cultures containing 10^7 microorganisms/mL. The diffusion time was 1 hr at 5°C and incubation time was 24 hr at 37°C for bacteria. Disc with only DMSO was used as control. Inhibitory activity was measured as the inhibition zones (diameter, mm).

Antifungal activity of aryl cinnamates 6a-e. The antifungal activity of aryl cinnamates **6a-e** was studied at a concentration (100 μg/disc) against two fungi, *viz*, *Asperigillus niger* and *Candida albicans*. For the detection of antifungal activity, the filter paper disc (6 mm disc) diffusion method was used. Griseofulvin (20 μg/disc) was used as standard antifungal agent. Nutrient agar (NA) was used as basal medium for test fungi. These agar media were inoculated with 0.5 mL of the 24 hr liquid cultures containing 10^7 microorganisms/mL. The diffusion time was 1 hr at 5°C and the incubation time was 7 days at 30°C for fungi. Disc with only DMSO was used as control. Inhibitory activity was measured as the inhibition zones (diameter, mm).

Results and Discussion

Antibacterial activity of cinnamyl cinnamates 5a-e. Antibacterial activity of cinnamyl cinnamates **5a** and **5d** have been studied at the concentration of 100 μg/disc against five human pathogenic bacteria. Among them one was Gram-positive (*S. aureus*) and rest four were Gram-negative bacteria (*E. coli, S. typhi, S. dysenteriae* and *S. soneii*). The inhibitory effects of cinnamyl cinnamates **5a** and **5d** against these organisms are depicted in **Table I**. The screening results indicate that cinnamyl cinnamates **5a** and **5d** showed antibacterial activity against all the bacteria tested. In general, the cinnamyl cinnamate **5a** exhibited better antibacterial activity than cinnamyl cinnamate **5d**. However, the activity of both these compounds was lower than the standard.

The same study was carried out with other three cinnamyl cinnamates **5b, 5c** and **5e** against ten human pathogenic bacterial species. Among them two were Gram-positive (*B. subtilis, S. aureus)* and the remaining eight were Gram-negative (*S. typhi, S. paratyphi A, S. paratyphi B, S. soneii, S. flexneri*, *P. aeruginosa*, *P. vulgaris*, and *E. coli*). Ampicilin (20 μg/disc) was used as standard antibacterial agent. The results are summarized in **Table II**.

In antibacterial bioassay, cinnamyl cinnamate **5c** was found to be more active against *Proteus vulgaris* followed by *Escherichia coli*. In general, cinnamyl cinnamate **5b** showed good antibacterial activity against *S. flexneri* and *S. aureus* followed by *S. sonnei*, *P. aeruginosa* and *P. vulgaris*. The cinnamyl cinnamate **5e** exhibited good antibacterial activity against *P. aeruginosa* followed by *S. typhi*. Amongst the test compounds cinnamyl cinnamate **5c** was found to be more active than compound **5b** followed by compound **5e**. However, the antibacterial activity of these compounds were lower than the standard.

Antifungal activity of cinnamyl cinnamates 5a and 5d. The antifungal activity of cinnamyl cinnamates **5a** and **5d** were studied against two human pathogenic fungi (*A. niger* and *C. albicans*). Both compounds were found to be totally inactive against these fungal species. However, other three cinnamyl cinnamates **5b, 5c** and **5e** reflected good antifungal activity against the same fungal species. The compound **5c** and **5e** exhibited equal antifungal potency against *A. niger*. Furthermore, compound **5e** reflected good activity against *C. albicans* followed by **5b**. However, both the compounds were found to be less active than the standard, Griseofulvin.

Antibacterial activity of aryl cinnamates 6a-e. Antibacterial activity of aryl cinnamates **6a-e** have been studied at a concentration of 100 μg/disc against ten human pathogenic bacteria. Among them two were Gram-positive (*B. subtilis* and *S. aureus*) and rest eight were Gram-negative bacteria (*S. typhi, S. paratyphi A, S. paratyphi B, S. soneii, S. flexneri*, *P. aeruginosa, P. vulgaris* and *E. coli*). The inhibitory effects of aryl cinnamates **6a-e** against these microorganisms are depicted in **Table IV**. The screening results indicated that aryl cinnamates **6a-e** showed antibacterial activity against all the bacteria tested. The compound **6b** exhibited higher antibacterial activity than **6d** and **6e** followed by **6a** and **6c**. However, the activity of these compounds was lower than the standard Ampicillin.

Table IV — Antibacterial screening for (*E*)-aryl cinnamates (**6a-e**)

Test Microorganisms Bacteria	**6a**	**6b**	**6c**	**6d**	**6e**	Standard drug Ampicillin
S. typhi	10.5±0.5	13.5±0.8	10.2±2	12.2±1.5	13.3±0.5	14.5±1
S. paratyphae A	13.1±1	2.3±0.5	13.2±0.5	—	11.5±2	15.3±1
S. paratyphae B	12.2±0.8	—	11.5±1	11.5±0.8	12.4±1	13.6±1
S. sonnei	—	13.1±0.6	12.6±1.5	13.4±1	12.2±0.5	16.3±1
S. flexneri	10.6±0.5	12.2±0.6	11.3±1	—	11.4±0.5	16.7±1
P. aeruginosa	10.4±0.8	—	12.2±0.5	13.4±0.5	—	19.5±1
B. subtilis	12.1±0.5	12.2±0.8	10.5±0.8	11.2±0.8	10.1±1	15.6±1
P. vulgaris	11.7±1	11.1±2	—	10.2±1	13.5±0.8	18.7±1
S. aureus	12.3±0.8	—	11.5±2	—	12.3±0.5	18.8±1
E. coli	—	11.1±1.5	—	10.2±1.2	—	17.9±1

Table V — Antifungal screening for (*E*)-aryl cinnamates (**6a-e**)

Test Microorganisms Fungi	**6a**	**6b**	**6c**	**6d**	**6e**	Standard drug Griseofulvin
A. niger	—	11.2±1.5	12.5±0.8	—	12.3±1	14.3±1
C. albicans	10.5±1	13.2±0.5	—	—	12.4±1	16.1±1

Antifungal activity of aryl cinnamate 6a-e. The antifungal activity of aryl cinnamates **6a-e** were studied against two human pathogenic fungi (*A. niger* and *C. albicans*). The inhibitory effects of aryl cinnamates **6a-e** against these organisms are depicted in **Table V**. The compound **6b** exhibited higher antifungal activity than **6e** against *C. albicans*, whereas, **6e** showed higher antifungal activity than **6b** against *A. niger*. However, both the compounds **6b** and **6e** were found to be less active than the standard, Griseofulvin.

Acknowledgement

One of authors (RPM) is thankful to North Maharashtra University for the award of Chief Minister Fund Fellowship.

References

1 Greenaway W, Wollenweber E, Scaysbrook T & Whatley F R, *J Chromatogr,* 448, **1988**, 284.
2 Kumazawa S, Hayashi K, Kajiya K, Ishii T, Hamasaka T & Nakayama T, *J Agric Food Chem*, 50, **2002**, 4777.
3 El Hady F K A & Hegazi A G, *Z Naturforsch*, 57c, **2002**, 386.
4 Greenaway W & Whatley F R, *J Chromatrogr*, 519, **1990,**145.
5 Amoros M, Lurton E, Boustie J, Girre L, Sauvager F & Cormier M, *J Nat Prod*, 57, **1994**, 644.
6 Kujumgiev A, Tsvetkova I, Serkedjieva Y, Bankova V, Christov R & Popov S, *J Ethnopharmacol*, 64, **1999**, 235.
7 Metzner J, Schneidewind E & Frienfinch E, *Pharmazie*, 32, **1977**, 730.
8 Wang L, Mineshita S, Ga I, Shigematsu T & Matsuno T, *Japan J Pharmacol Ther,* 24, **1993**, 223.
9 Matsuno T, *Z Naturforsch* , 55c, **1995**, 93.
10 Baslas K K & Deshapande S S, *J Indian Chem Soc,* 27, **1950**, 379.
11 Opdyke D L J, *Food Cosmet Toxicol* 13, **1975,** 753.
12 Huang P, Yang M, Lai M, Zheng X, Nishi M & Nakanishi T, *J Chin Pharm Sci*, 6, **1997**, 129.
13 Zhang L P & Ji Z Z, *Yaoxue Xuebao*, 21, **1993**, 817; *Chem Abstr*, 118, **1992**, 212590x.
14 Tawata S, Taira S, Kobamota N, Zhu J, Ishihara M & Toyama S, *Biosci Biotech Biochem*, 60, **1996**, 909.
15 Shin J S, Kim J H, Park J H, Son E-D, Park H-G & Kim B-K, *Soul Taehak Yakh Nonmu*, 21, **1996**, 1; *Chem Abstr*, 130**, 1999**, 76142w.
16 Shi M, Wang C J & Chan A S C, *Tetrahedron: Asymmetry*, 12, **2001**, 3105.
17 Oida T, Tanimoto S, Ikehira H & Okano M, *Bull Chem Research*, *Kyoto University*, 60, **1982**, 336.
18 Moghaddam F M, Ghaffarzadeh M G & Abdi-Oskoui S H, *J Chem Res(S)*, **1999**, 574.
19 Khanna K S, Garg C P & Kapoor R P, *Org Prep Proc Int,* 24, **1992**, 469.
20 Pinto C G A, Silva A M S & Cavaleiro J A S, *Tetrahedron*, 55, **1999**, 10187.
21 Chamchaang W, Chantarasiri N, Chaona S, Thebtaranonth T & Thebtaranonth Y, *Tetrahedron*, 40, **1984**, 1727.
22 Nishikubo T, Takahashi E, Miyaji T & Iizawa T, *Bull Chem Soc Japan*, 58, **1985**, 3399.
23 Manimaran T & Ramkrishnan V T, *Indian J Chem*, 18B, **1979**, 324.

24 Shankaran K, Sloan C P & Snieckus V, *Tetrahedron Lett,* 26, **1985**, 6001.
25 Nagamura S, Asai A, Amishiro N, Kobayashi E, Gomi K & Saito H, *J Med Chem*, 40, **1997**, 972.
26 Nagamura S, Saito H, Kobayashi E & Gomi K, *Eur Pat Appl EP* 520435 A2 30 Dec **1992**; *Chem Abstr*, 118, **1993**, 191718c.
27 a) Mahajan R P, Patil S L & Mali R S, *Indian J Chem,* 45B, **2006**, 328; b) Mahajan R P, Patil S L & Mali R S *Org Prep Proc Int,* 37, **2005**, 286; c) Westmann J, *Org Lett*, 3, **2001**, 3745; d) Valizadeh H, Shockravi A, Heravi M M & Ghadim H A, *J Chem Res* **2003**, 718.
28 Mali R S & Papalkar A S, *J Chem Res (S),* **2001,** 433.
29 Mali R S & Papalkar A S, *J Chem Res*, **2003**, 603.
30 Asakawa Y, *Bull Chem Soc Jpn*, 45, **1972**, 1774.
31 a) Rollas S, Kalyoncuoglu N, Sur-Altiner D & Yegenoglu Y, *Pharmazie,* 48**, 1993**, 308; b) Bauer A W, Kirby W W M, Sherris J C & Turck M, *Am J Clin Pathol,* 45, **1966**, 493.