General summary

Clerodendrum is a very large and diverse genus and are widely distributed in Asia, Australia, Africa and America.

The present study includes the following:

Part I: Phytochemical study includes preliminary phytochemical screening of certain *Clerodendrum* species and investigation of the contents of ethyl acetate, *n*-butanol fractions and dichloromethane extract of *C. chinense* (Osbeck) Mabb.

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Part II: Biological study of different *Clerodendrum* species and isolated compounds.

Part I: Phytochemical study of certain *Clerodendrum* species:

Chapter I: Preliminary phytochemical screening:

Preliminary phytochemical screening of the leaves of *C. chinense*, *C. indicum and C. glabrum* revealed the presence of carbohydrates and/or glycosides, sterols and/or triterpenes, tannins and free flavonoids in all the leaves of the plants under investigation. Especially *C. chinense* contains appreciable amount of free flavonoids. Flavonoid glycosides are present in the leaves of *C. chinense* and *C. glabrum* and large amount in *C. indicum*.

Chapter II: Investigation of the contents of dichloromethane extract of *C. chinense* (Osbeck) Mabb.:

The air-dried powdered leaves were macerated in dichloromethane until exhaustion. The extracts were evaporated under reduced pressure at

low temperature to yield a residue. The residue was decolorized by dissolving it in methanol and adding activated charcoal followed by warming in water bath then filter. The filtrate was evaporated under reduced pressure at a low temperature to yield a yellow residue. The residue was chromatographed on silica gel column using gradient elution with *n*-hexane and increasing the polarity with ethyl acetate till 100% ethyl acetate then increasing the polarity by methanol. Two main fractions were collected. First one is almost pure compound and the second subjected for further purification through silica gel column and preparative TLC. Comparing our finding with those cited in the literature, the identified compounds were identified by different spectral techniques as the following:

D_1: Lupeol

D_2: Rengyolone (Cleroindicin F)

Chapter III: Investigation of the contents of ethyl acetate fraction of *C. chinense* (Osbeck) Mabb.:

The air-dried powdered leaves were macerated in 80% aqueous methanol until exhaustion. The extracts were evaporated under reduced pressure at low temperature to yield a residue. The residue was dissolved in water and left over night in a refrigerator and filtered. The filtrate was extracted with successive portions of chloroform, ethyl acetate and *n*-butanol till exhaustion. All similar portions were combined and evaporated under reduced pressure to yield semisolid residue from chloroform, ethyl acetate and *n*-butanol fractions respectively. The ethyl acetate residue was fractionated on chromatographic silica gel column using gradient elution with *n*-hexane and increasing the polarity with ethyl acetate. The fractions were monitored by TLC using solvent system ethyl acetate : hexane (7.5 :

2.5) and similar fractions were pooled. First fraction was rechromatographed on chromatographic silica gel to get one compound. Second fraction was rechromatographed on polyamide column to get two main fractions which separately purified on RP C_{18} column. Two compounds were isolated. Comparing our finding with those cited in the literature, the identified compounds were identified by different spectral techniques as the following:

L_1: Hispidulin

L_2: Verbascoside

L_3: Isoverbascoside

Chapter IV: Investigation of the contents of *n*-butanol fraction of *C. chinense* (Osbeck) Mabb.:

The *n*-butanol residue was fractionated on polyamide column using water with increasing the percent of methanol. The fractions were monitored by TLC using solvent system ethyl acetate : formic acid : acetic acid : water (30 : 1.2 : 0.8 : 8) and similar fractions were pooled. Three main fractions were collected. Both of them were separately purified by RP chromabond C18 $_{ec}$ using water and acetonitrile to isolate two compounds. The remaining fractions subjected to RP chromabond $C_{18\ ec}$ using water, RP C18 column using water and acetonitrile and preparative RP TLC plate using water : acetonitrile : acetic acid (94 : 2 : 4) to isolate one compound. Comparing our finding with those cited in the literature, the identified compounds were identified as the following:

B_1: Cornoside

B_2: Decaffeoyl verbascoside

B_3: Icariside B_5

Part II: Biological study of *Clerodendrum* species.

Chapter I: *In vivo* pharmacological studies of alcoholic, chloroformic and aqueous extracts of leaves of *C. chinense, C. indicum, C. splendes and C. glabrum* as well as of isolated verbascoside:

a) Toxicological studies:

The tested extracts and purified verbascoside are more or less safe.

b) Acute anti-inflammatory effect:

The rat groups administrated the methanolic extract of leaves of *C. chinense* and *C. indicum* in an oral dose of 100 mg/Kg b. wt. and verbascoside in an oral dose of 25 mg/Kg b. wt. showed highly significant anti-inflammatory effect that was found to be about 77- 89 % of the effect of indomethacin after 4 hours. The rat groups administrated the chloroformic extract of leaves of *C. chinense* and methanolic extract of leaves of *C. glabrum* in an oral dose of 100 mg/Kg b. wt. showed significant anti-inflammatory effect that was found to be about 56- 63 % of the effect of indomethacin after 4 hours. Chloroformic extracts of leaves of both *C. indicum and C. glabrum* showed less anti-inflammatory effect at an oral dose of 100 mg/Kg b. wt.

c) Analgesic effect:

The rat groups administrated the methanolic extract of leaves of *C. chinense* in an oral dose of 100 mg/Kg b. wt. and verbascoside in an oral dose of 25 mg/Kg b. wt. showed highly significant analgesic effect that was found to be about 74- 89 % of the effect of novalgin after 1 hour and about 61- 73 % of novalgin activity after 2 hours. All other groups showed less analgesic effect at an oral dose of 100 mg/Kg b. wt.

d) Antipyretic effect:

The rat groups administrated the methanolic extract of leaves of *C. chinense* in an oral dose of 100 mg/Kg b. wt. and verbascoside in an oral dose of 25 mg/Kg b. wt. showed highly significant antipyretic effect that was found to be about 58- 73 % of the activity of paracetamol after 1 hour and about 67- 81 % of paracetamol effect after 2 hours. The rat group administrated the methanolic extract of leaves of *C. glabrum* in an oral dose of 100 mg/Kg b. wt. showed significant anti-inflammatory effect that was found to be about 57 % of the effect of paracetamol after 1 hour and about 55 % of paracetamol effect after 2 hours. The rat group administrated the methanolic extract of leaves of *C. indicum* in an oral dose of 100 mg/Kg b. wt. showed less antipyretic effect**.** The rat groups administrated the chloroformic extracts of leaves of both *C. indicum* and *C. glabrum* showed non significant antipyretic effect at an oral dose of 100 mg/Kg b. wt.

e) Antioxidant activity:

The aqueous extracts of the leaves of both *C. chinense* and *C. indicum* in an oral dose of 100 mg/Kg b. wt. as well as verbascoside in an oral dose of 25 mg/Kg b. wt. showed highly antioxidant effect comparable with methanolic extract of the same dose.

Chapter II: Antimicrobial and cytotoxic effects of alcoholic and chloroformic extracts of different plant organs of *C. chinense, C. indicum*, *C. splendes* and *C. glabrum* as well as some of the isolated compounds:

The choroformic extracts of different parts of different *Clerodendrum* species showed variable extent of antiprotozoal effect. Different chloroformic extract show marginal effect against *L. inflatum* but more

powerful effect against *P. falciparum* especially chloroformic extracts of flowers of both *C. chinense* and *C. splendes* where IC_{50} < 10 µg/ml. The chloroformic extracts of stem and flower of *C. chinense* are very active against *T. cruzi* with marginal cytotoxicity. The chloroformic extracts of leaves of both *C. chinense* and *C. splendes* have promising effects against *T. cruzi* without cytotoxic effect on human cell line and this suggest the selectivity of those two extracts against *T. cruzi.*

The methanolic extracts of different parts of different *Clerodendrum* species are less active against parasites comparable with the effect of chloroformic extracts.

Verbascoside show marginal effect against *T. cruzi*. Isolated rengyolon shows a broad but non specific effect, related to its general cytotoxicity.

Methanolic extract of leaves of *C. chinense* show marginal effect against *Microsporum canis.* Other extracts and isolated compounds did not show antibacterial or antifungal effects.