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Research Article

**PHENOLIC CONTENTS, CYTOTOXICITY AND
ANTIMICROBIAL ACTIVITY OF FIVE MEDICINAL PLANTS
OF THE LAMIACEAE FAMILY OBTAINED FROM SAUDI
ARABIA LOCAL MARKETS****Hasan Yusufoglu^{1,*}, Ahmed I. Foudah¹, Mohammed Alqarni¹, Aftab Alam¹, Mohammed Ayman Salkini¹, Elmutasim O. Ahmed²**¹Department of Pharmacognosy, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj, KSA.²Department of Pharmaceutics, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj, KSA**Abstract:**

Leaves of *Salvia officinalis*, *Rosmarinus officinalis*, *Thymus vulgaris*, *Origanum syriacum*, and *Lavandula angustifolia* were purchased from Riyadh (Saudi Arabia) local market, evaluate physicochemical limits and prepared the methanolic extracts. The total phenolic contents (TPC) of extracts were evaluated using Folin-Ciocalteu reagent, all the extracts showed good quantity of TPC and the decreasing orders were shown as *R. officinalis*, *T. vulgaris*, and *L. angustifolia*, *O. syriacum* and *S. officinalis*. Antimicrobial activity was evaluated using the disk diffusion method and all the selected herbs were exhibited some degree of antimicrobial activity. Out of five extracts, three (*R. officinalis*, *T. vulgaris*, and *L. angustifolia*) were found to be the most active agents against *B. subtilis*, *K. pneumonia* and *C. albicans*. The cytotoxicity was evaluated using MCF-7 human breast cancer cell lines, and the extract from *R. officinalis* was confirmed the most auspicious cytotoxic agents followed by *T. vulgaris*, and *L. angustifolia* respectively. Present study, concluded that the extracts of Rosemary, Thyme, and Lavender had a good quantity of phenolic contents, these extracts could be a potent source of antibiotics and effective cytotoxic agents against MCF-7 human cells.

Keywords: Lamiaceae herbs, phenolic, antimicrobial, cytotoxic, MCF-7, KSA**Corresponding author:****Prof. Dr. Hasan Soliman Yusufoglu,**

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INTRODUCTION:

The Lamiaceae (Mint family, cosmopolitan in nature) is the largest family (sixth rank) of flowering plants; containing about 236 genera and around 7000 species. Plants of this family are very important commercially due to the culinary, beautiful flower, aromatic qualities, essential oils and medicinal properties [1]. Members of Lamiaceae family have been recently divided into ten subfamilies, among the subfamily, Nepetoideae is the largest, containing almost half of the total species; further Nepetoideae is divided into three tribes (Elsholtzieae, Mentheae, and Ocimeae). The Mentheae is the largest tribe and it represents genera i.e. Mentha, Melisa, Origanum, Rosmarinus, Salvia, and Thyme and Ocimeae are the second largest tribe. Among the tribes, Mentheae represents economically important genera such as Lavandula and Ocimum [2]. The extracted essential oils of Mentheae and Ocimeae tribe are commonly used as flavour and fragrance in the food, cosmetics, perfumery, and pharmaceutical industries [3]. Lamiaceae family is well represented in the flora of Saudi Arabia, where 76 species, and among them 23 species are medicinal plants [4]. In the Sarrwat Mountains of Taif (Saudi Arabia) 14 species belongs to the 9 genera i.e. Lavandula (2), Mentha (2), Salvia (3), Marubium (1), Leucas (1) Ocimum (1), Micromeria (2) Otostegia (1) Teucrium (1) have been invented [5]. The medicinal uses of Lamiaceae family plants are common between the locals of Saudi Arabia for the treatments of common ailments [6,7]. Among the medicinal plants used in the Makkah region of Saudi Arabia, Lamiaceae positioned third rank in the recent Ethnopharmacological survey [8]. The leaves of the Lamiaceae plants have been reported for the treatments in the antiseptic, anti-scabies, anti-syphilitic, antioxidants, and anti-inflammatory conditions [9-11]. The uses of herbal medicine for maintaining the health are common in Saudi Arabia, so, there is a need to test the marketed plants for their safety, efficacy, acceptability and effectiveness [12]. The analysis of phenolic content is one of the important parameters for the standardization and quantification of active composition in the medicinal plants [13]. In Saudi Arabia, medicinal plants are mostly available in the local markets without any safety and efficacy label, So the purpose of the present study was to evaluate the phenolic contents, antimicrobials, and Cytotoxic efficacy of *O. syriacum*, *R. officinalis*, *S. officinalis*, and *T. vulgaris* leaves purchased from the local market of Al-Riyadh (KSA)

MATERIALS AND METHODS:

Plant material: Purchase, Grind, and physicochemical study

Dried leaves of five plants Salvia (*S. officinalis* L), Rosemary (*R. officinalis* L), Thyme (*T. vulgaris* L), Oreganos (*O. syriacum* L), and Lavender (*L. angustifolia* Mill) were purchased from the local market of Batha, Centre of Riyadh (KSA). Specimens were authenticated by Dr. Osman A. Elmakki using the morphological features. The voucher specimens were deposited at the herbarium, College of Pharmacy as; Salvia (PSAU-03-CPH-2017), Rosemary (PSAU-05-CPH-2017), Thyme (PSAU-06-CPH-2017), Oreganos (PSAU-07-CPH-2017), and Lavender (PSAU-09-CPH-2017), at Prince Sattam Bin Abdulaziz University, Riyadh, KSA. The dried leaves of the selected plants were powdered using a grinder separately and used for the physicochemical studies such as the total ash, moisture and extracting contents using reported methods [14].

Methanolic extract: Preparation and study of preliminary phytochemicals and total phenolic content (TPC)

The powder of each specimen (100 g) was separately extracted using macerated method [15]. The extraction was repeated three times with the same plant and the filtrates were collected together. Latter, filtrates were transferred to a rotary evaporator (at temperature-40° C, rpm-100, and pressure- 150mbr) to separate the solvent. The dried methanolic extracts of all the Lamiaceae members were studied for the preliminary phytochemicals using reported methods [16] and total phenolic contents (TPC) following the Folin-Ciocalteu reagent method [17]. Total phenolic contents were stated in mg Gallic acid equivalents (GAE) per g dry extract (DW).

In-Vitro cytotoxic potential of the selected Lamiaceae plant extracts

The in vitro cytotoxic study of the methanol of the selected Lamiaceae family were evaluated using MTT [3-(4, 5- Dimethylthiazol-2-yl) - 2, 5- Diphenyl-tetrazolium Bromide] Assay [18]. Human cancer cell line: MCF-7 (Breast) was grown in DMEM media supplemented with 10% bovine serum, 1X penicillin-streptomycin (Sigma-Aldrich) at 37°C in a humidified chamber with 5% CO₂. The Cells were seeded (1X10⁵ cells/well in triplicate) in a 96-well flat-bottom plate (Becton-Dickinson Lab ware) a day before treatment and grown. Stocks of all extracts (2.0 mg/ml) were made with 5% DMSO (Sigma-Aldrich) and further working solutions (100 mg/ml) were prepared in serum-free culture media. Cells were treated with four different doses (5, 10, 20, and 30 mg/ml; in triplicate) of the compounds in complete growth media and it was further incubated for 48 hours. On day 2 of treatment, MTT test was performed using TACS MTT

Cell Proliferation and Viability Assay Kit (TACS) as per manufacturer's instructions. The relationship between surviving fraction and compound concentration was plotted to obtain the survival curve of cancer cell lines. The response parameter calculated was the IC₅₀ value, which corresponds to the concentration required for 50% inhibition of cell viability.

In-vitro antimicrobial activity of the selected Lamiaceae plant extracts

The in vitro antimicrobial activities of the extracts of selected Lamiaceae plants were evaluated by disc diffusion method [19]. The media Mueller-Hinton agar (MHA) and Sabouraud Dextrose agar (SDA) were used for bacteria and fungi respectively. The microorganisms, Gram-positive (*Bacillus subtilis* (ATCC 10400), Gram negative *Klebsiella pneumonia* (ATCC 13882) and *Candida albicans* (NCYC 1363) were used for the antimicrobial activities. Amoxicillin (10 µg/ml) was used as positive controls. The discs containing 30µL of the methanol extracts of Salvia, Rosemary, Thyme, Origanum, and Lavandula were used as samples and the zone of microorganisms

growth inhibition around the disc were measured after 24h incubation and 48h incubation at 37°C and 24°C for bacteria and fungi, respectively.

Statistical Analysis: Results are reported as the means $\pm$ SD. The correlation between analysis of antioxidant activity and the total phenolic and flavonoid contents were carried out using the correlation and regression applications in the Microsoft Excel.

RESULTS:

Physicochemical study

In the present study, it was observed that, the total ash contents of selected Lamiaceae species were varied in between 8.83% to 10.68%, the highest total ash was shown in the leaves of Thyme and lowest in Rosemary (Table 1). The moisture contents of leaves were varied in between 4.74% to 6.85%. The high soluble contents were shown in the methanolic extract as compared to the hexane and ethyl acetate soluble contents (Figure 1). The contents (%) of methanolic extract were varied in between 10.12% to 14.62%, the highest content was found in Thyme and lowest in Oreganos.

Table 1. Total ash and moisture contents of powder of selected Lamiaceae members.

Plants of Lamiaceae family	Total ash (%w/w)	Moisture contents (%w/w)
Salvia	8.83	5.99
Rosemary	8.01	5.76
Thyme	10.68	5.44
Syrian Oregano	9.22	4.99
Lavender	10.06	6.55

Average value (% of w/w) of three repeated experiments

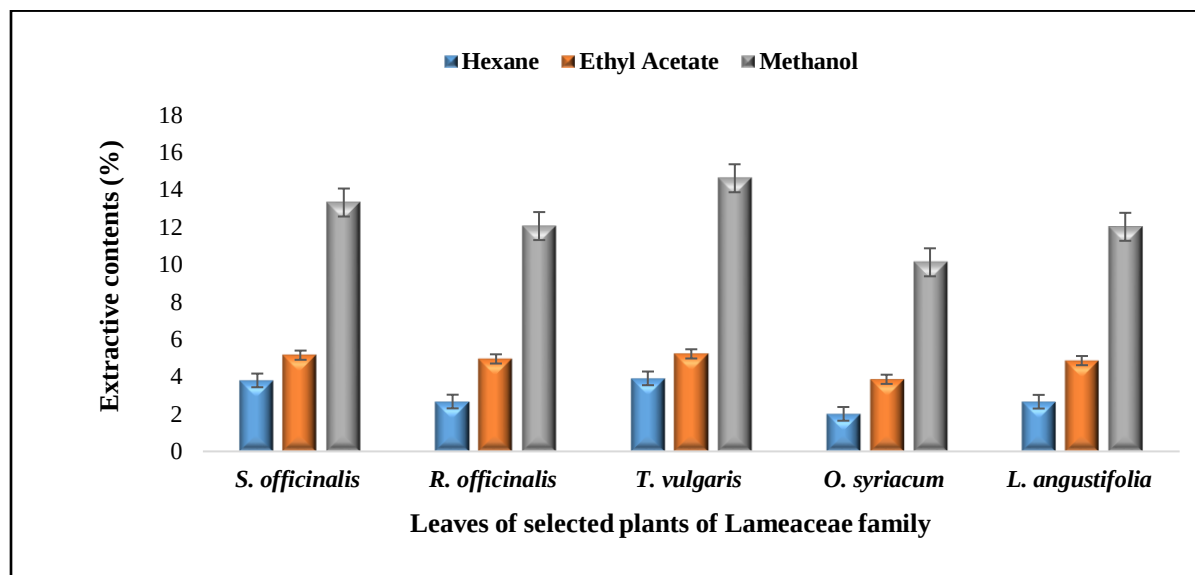


Figure 1. Percentage extractive contents of powder of selected Lamiaceae members.

Phytochemicals and total phenolic content (TPC)

The phytochemical analysis of the methanol extracts of Salvia, Oreganos, Lavender, Rosemary, and Thyme for the presence of alkaloids, carbohydrates, reducing sugars, phenolic & flavonoids, phytosterols, glycoside, tannins, and protein & amino acids and the results were reported in Table 2. Total phenolic contents (TPC) of the extracts were represented in Figure 2. The quantity of TPC in the extracts were ranged from 55.6 to 108.2mgGAE/g DE. The highest TPC was found in the Rosemary extract and the lowest was found in the Salvia extract.

Table 2. Phytochemicals study of methanol extract of selected plants of Lamiaceae family.

Chemical tests	Methanolic extract				
	Salvia	Rosemary	Thyme	Oreganos	Lavender
Mayers (Alkaloids)	+	+	+	+	+
Wagner's (Alkaloids)	-	++	+	-	+
Molisch's (Carbohydrates)	+	+	+	+	+
Fehling (reducing sugar)	-	++	+	+	+
FeCl ₃ (10%) (Phenolic)	+	+++	++	+	++
Alkaline reagent (Flavonoids)	+	+++	+++	+	++
Salkowski's (Phytosterols)	+	+	+	+	+
Mod. borntrager's (Glycosides)	+	++	++	+	++
Ferric-chloride (1%) (Tannins)	+	++	++	+	+
Ninhydrin (Amino acids)	+	+	+	+	+

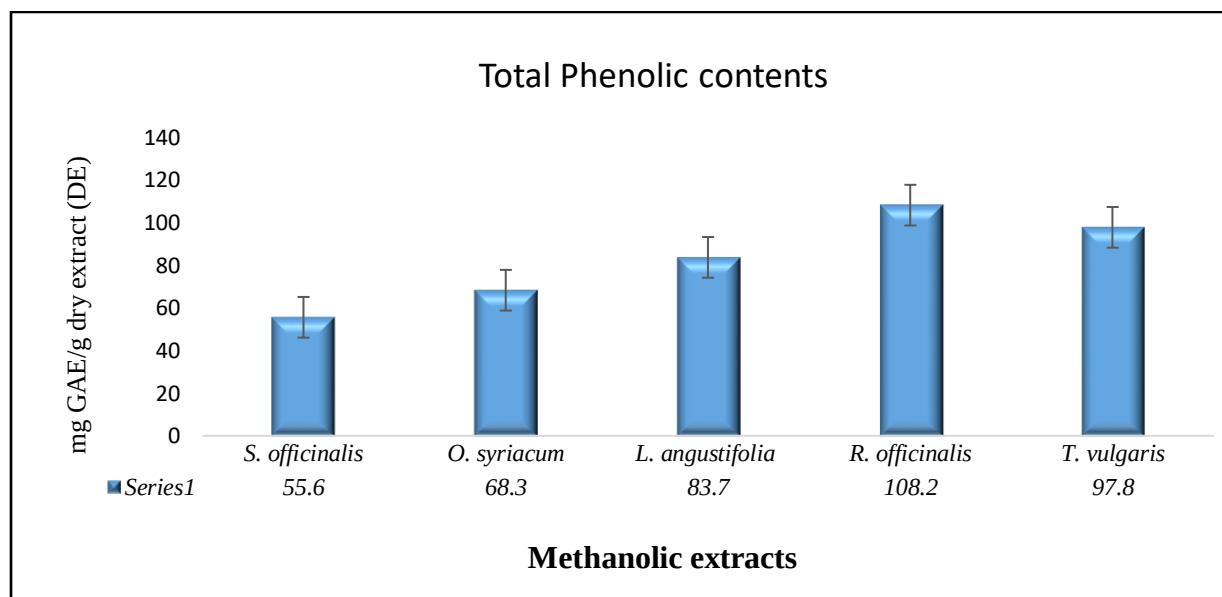


Figure 2. TPC of methanolic extract of selected plants of Lamiaceae family.

In-Vitro Cytotoxic study

The extracts of selected members of Lamiaceae were evaluated against a human cancer cell lines, MCF-7 (Breast) and the results were summarized in Table 3. Cells were treated with the test extracts with different concentrations (5, 10, 20 and 30 µg/ml) in the triplicate, for 48 h. The results of the tested extracts against the MCF-7 cell line were expressed in IC₅₀ values.

In-vitro antimicrobial activity

In the present study, the extracts of Salvia, Oreganos, Lavender, Rosemary, and Thyme were showed high inhibitory action against *B. subtilis* (12, 13, 14, 18 and, 15 mm, respectively) and intermediate against *K. pneumoniae* and (10, 11, 11, 13 and 12 mm, respectively), and low activity against *C. albicans* (9, 10, 10, 11, 11 mm, respectively) (Table 4).

Table 3. IC50 values of methanolic extracts of selected members of “Lamiaceae” family against a human cancer cell lines (MCF-7)

Methanolic extract of Lamiaceae leaves	MCF-7 (Breast) (IC-50)
Salvia	60.70 ± 5.4µg/ml
Rosemary	18.01 ± 1.7µg/ml
Thyme	24.73 ± 2.5µg/ml
Syrian Oregano	45.85 ± 4.2µg/ml
Lavender	35.11 ± 3.5µg/ml

Table 4: Antimicrobial study by agar diffusion method (mm) of methanol extract of selected members of “Lamiaceae” family

Methanolic extract of Lamiaceae Members (30mg/ml)	Zone of Inhibition (mm)		
	<i>B. subtilis</i>	<i>K. pneumonia</i>	<i>C. albicans</i>
Salvia	12 ± 0.28	10 ± 0.32	9 ± 1.02
Rosemary	18 ± 0.11	13 ± 0.24	11 ± 0.44
Thyme	15 ± 0.54	12 ± 0.42	11 ± 0.32
Syrian Oregano	13 ± 0.54	11 ± 0.42	10 ± 0.32
Lavender	14 ± 0.28	11 ± 0.32	10 ± 0.52
Amoxicillin (1mg/ml)	20 ± 0.84	18 ± 0.74	16 ± 0.16

re the “mean ± SD” of three repeated experiments. NA=not active (Less than 8mm), mm= millimeter and all the values were “mean ± SD” of three repeated experiments.

DISCUSSION:**Physicochemical study**

Physicochemical properties of medicinal plants play a very important role in detecting the purity or efficacy. The ash (11.91 to 12.57%) and moisture (8.14-2.13) contents of the Jordanian *S. officinalis* leave has been reported, different from the present reported Saudi marketed Salvia leaves [20]. A range of total ash (9.28 to 13.51%), moisture contents (4.47 to 8.93%) and methanol contents (9.63 to 15.56%) have been reported for Indian rosemary, similar to that our present finding [21]. WHO monograph on thyme leaves mentioned not more than 10% moisture and not more than 15% total ash and the ranges of present selected thyme was in the WHO monograph range [22]. For the oreganos, the present the total ash and moisture contents reports were similar to that of México oreganos total ash (7.58 to 8.43%) and moisture (3.15 to 7.12%) contents range [23]. The moisture (6.80%) and ash (7.49%) contents reported for the Pakistan lavender is nearly similar to the present result.

Phytochemicals and total phenolic content (TPC)

In the present study, the phytochemical screening of extracts was revealed the presence of active constituents with variable intensity. The presence of phenolic, flavonoids and glycosides were found to be more in *Rosemary*, *Thyme*, and *Lavender* in comparing to the *Salvia* and *Oreganos*. The vast variations in the flavonoids, phenolic acids, terpenes, and terpenoids among the plants have been suggested to be responsible for the variations in biological activities [24-25]. TPC of Lamiaceae species (*Lavender*, *Salvia*, *Oreganos*, *Rosemary*, and *Thyme*) from Romania ranged between 40-87.8 mg GAE/g dry extract is comparatively higher than the TPC (14.53-33.22 mg GAE·g⁻¹) from Iran Lamiaceae species [26-27]. The present results as shown in Figure 2, the total phenolic content ranges from 55.6-108.2mg GAE/g dry extract (comparatively higher than Romania and Iranian Lamiaceae species).

Cytotoxic study

In woman, breast cancer is the most severe type of malignancies, has the metastasis potential, and one of

the leading cause of cancer-related deaths [28]. In vitro cytotoxic potential of extracts at a concentration of 5 to 30mg/ml against MCF-7 (Breast) human cancer cell lines have been assessed in present study. The results revealed that all the extracts were shown anti-proliferative activity against MCF-7 human breast cancer cell lines but with different degrees. A study on MCF-7 (human, breast, adenocarcinoma) reported that Rosemary extract is a potential candidate for cytotoxic activity [29]. A significance inhibition against MCF-7 human breast cancer cells due to the high content of phenolic and flavonoids by thyme extract have been already reported [30]. The alcoholic extract of Oreganos was found to be more active against MCF7-human breast cancer cells due to high contents of phenolic, tannins and flavonoids [31]. A previous study has been reported, that extract of Salvia had significant cytotoxic potential against human breast MCF-7 [32]. Recently, Tabatabaei *et al.*, [33], demonstrated that the essential oils of Thyme lavender and Rosemary against MCF-7 human breast cancer cell lines and reported that Thyme oil was more potent to inhibit MCF 7-cancer cell as compare to Rosemary and Lavandula oils. In present finding, the extracts of Rosemary, Thyme and Lavender were found to be more efficient in inhibiting cell proliferation compare to Salvia and Oreganos.

Antimicrobials potential

The antimicrobial activities of methanol extracts of Salvia, Oreganos, Lavandula, Rosemary, and Thyme against *B. subtilis*, *K. pneumonia*, and *C. albicans*, have been assessed in the present study. The results revealed that the extract of all plants was efficiently suppressed the growth of microorganisms with variable potency. As stated, (Table 4) extract of Rosemary had the maximum zone of inhibition against *B. subtilis*, *K. pneumonia* and *C. albicans*, whereas Salvia showed less active. It has been previously reported that, the alcoholic extract of oreganos, lavender, rosemary, and thyme exhibited inhibitory effects against food spoilage bacteria (Gram-positive and Gram-negative), as well as fungi [34-36]. The lower antimicrobial activities of extracts may be due to the inferior quality of plants or less the content of phenolic, flavonoids or other active compounds. In present finding, all the extracts were highly active against *B. subtilis* and comparatively low active against *C. albicans*.

CONCLUSIONS:

According to the results obtained in the present study, the differences in cytotoxic and antimicrobial activities of the extracts may be due to the presence of phenolic or other active compounds. It is well-known

that phenolic compounds contribute to the quality of health-beneficial effects. Among the five studied plants, the order of phenolic, cytotoxic, and antimicrobials in the extract were found in the order of, Rosemary, Thyme, Lavender, Oreganos, and Salvia. Hence, Rosemary was found to be the most promising inhibition of MCF-7 cell proliferation of breast cancer and selected microbes, following the thyme and lavender.

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CONFLICT OF INTEREST

No conflict of interest declared by author.

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