In Vitro, Evaluation of Anticancer and Anti-dermatophytes Activities of Some Egyptian Medicinal Plants

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Abstract

In this investigation three ancient Egyptian medical plants; *Plantago albicans* L., *Thymelaea hirsuta* (L.) Endl. and *Urginea maritima* (L.) were chosen to explore their biochemical properties, anticancer and antimycotic activities against clinical dermatophytes. Growing of *Trichophyton soudanense*, *Trichophyton erinacei*, *Microsporum audouinii*, *Microsporum gypseum*, *Microsporum gallinae*, *Microsporum ferrogenium*, *Microsporum cookie*, *Microsporum racemosum*, *Microsporum persicolor* and *Microsporum canis* were totally inhibited by the 100 µg/mL of *P. albicans* methanolic extract. Whereas the growth of *T. soudanense*, *T. erinacei*, *Trichophyton rubrum*, *Trichophyton tonsurans* and *Trichophyton mentagrophytes* and *Epidermophyton floccosum* were 100% inhibited by the methanolic extract of *T. hirsuta* at 100 µg/mL concentration, however its acetone extract was more active against *Microsporum* species. The highest fungi toxicity against all dermatophytic fungi was detected in both methanol and acetone extract of *U. maritima* at a concentration ranged between 50 to 100 µg/mL. Methanolic extract of *P. albicans* inhibited the viability of HCT-116, HepG-2, MCF-7 and HeLa cell lines by (41%, 40%, 80% and 81%); (30%, 20%, 66% and 70%); (19%, 0%, 49% and 57%); (5%, 0%, 35% and 45%) and (0%, 0%, 21% and 40%) at 25, 50, 100, 200 and 300 µg/mL, respectively. Moreover, the cells death after treatment with the same concentrations of *T. hirsuta* methanol extract were (10%, 20%, 23% and 60%); (16%, 40%, 58% and 80%); (40%, 50%, 80% and 100%); (51%, 65%, 100% and 100%) and (49%, 82%, 100% and 100%) in HCT-116, HepG-2, MCF-7 and HeLa cells, respectively. Viability of HCT-116, MCF-7 and HepG-2 cell lines was totally suppressed with 100 µg/mL whereas the HeLa cell growth was reduced to 10% and totally killed at 100 and 200 µg/mL, respectively of *U. maritima* methanolic extract. All data approve the significance of Egyptian ethnomedical plants as potent source of diverse bioactive pharmaceutical metabolites.

Introduction

Dermatophytes are keratinophilic fungi include *Trichophyton*, *Microsporum* and *Epidermophyton* genera, which exclusively penetrates the tissues of stratum corneum, nails or human hair by means of enzymatic and non enzymatic virulence factors like keratinases, proteases, phospholipases and cellulases and then infection occurs (El-Gendy et al. 2014; Van et al. 2019). Based on the World Health Organization (WHO), cancer is one of the principal reasons of morbidity and mortality with ~14 million new cases and 8 million deaths and it is expected to increase this burden to 75, 27, and 17 millions cancer prevalent, incident and deaths respectively by 2030 (Alves-Silva et al. 2017). In Egypt occurrence rates per 100,000 were 166.6 in both sexes, 175.9 in males and 157.0 in females. Most common cancer types in both sexes were liver, breast, and bladder cancers compared to liver and bladder cancer in men (33.6% and 10.7%, respectively) as well as breast (32.0%) followed by liver cancer (13.5%) in females (Ibrahim et al. 2014; El-Gendy et al. 2017, 2018a).

Interestingly dermatomycosis and dermatophytosis diseases by dermatophytic fungi remains a serious problem in cancer patient that is more threatening because of the emergence of immunosuppressive disease and multidrug resistant disease, so it is necessary to explore inexpensive and abundant natural alternatives (Sepahvand et al. 2018). Owing to environment diversity in Egypt, the traditional pharmacopoeia contains a vast resource of therapeutic plants that have long been used in folk medication for the treatment of numerous diseases as documented on the walls of temples and papyrus for example, the well-known Ebers Papyrus in 1550 B.C. reported 876 medicaments with 328 diverse constituents derived from numerous plant species (El-Demerdash 2018).

In Egypt, *P. albicans*, *T. hirsuta* and *U. maritima* are medicinal plants endemic to Egypt, grow in the coastal Mediterranean region, commonly used for its biological properties including anti-ulcerogenic, anti-inflammatory, antiangiogenic, antimalarial, anticancer, immunomodulatory, wound healing, antioxidant, antibacterial, antihypoglycaemic, hepatoprotective, hyperlipidemic, haemopoietic and cytotoxic activities (Elghuol et al. 2016; Nofal et al. 2016; Felhi et al. 2017) which attributed to their higher content of flavonoids, glycosides, tannins, reducing compounds, anthraquinones, anthocyanins, mucilage, polysaccharides, fatty acids, triterpenes and steroids in traditional medicinal (Elghuol et al. 2016; Belhadda et al. 2017).

The goal of current work was therefore to explore the biochemical characteristics of the ancient Egyptian medicinal plants, *T. hirsuta*, *P. albicans* and *U. maritima* as well as to evaluate for the first time their antimycotic activity against dermatophytes and anticancer activity against cell lines to develop our knowledge of the Egyptian plant as a cheap source of pharmacological agents that can protect the human from invasive dermatophytes and lethal cancer diseases. To the best of our knowledge, this study reports for the first time the efficiency of the ancient Egyptian medicinal plants, *P. albicans*, *T. hirsuta* and *U. maritima* as pharmaceutical agents against dermatophytes.

Materials And Methods

Chemicals

All chemicals were obtained from Sigma-Aldrich Chemicals Co. (St. Louis, MO) and Merck (Darmstadt, Germany).

Isolation and characterization of clinical dermatophytes

Isolation and characterization of dermatophytic fungi isolates from clinical samples were done as described by Rebell and Taplin (1970), Rinaldi et al. (1973), Merz and Roberts (1995), Kane et al. (1997), Larone (2002), Gromadzki et al. (2003), Koneman (2006), El-Gendy et al. (2010 and 2014) and El-Bondkly et al. (2012). The selectivity and efficiency of different detection methods including microscopic method by using 20% potassium hydroxide (KOH) and culture methods on different isolation media including rapid sporulation medium (RSM), Sabouraud dextrose agar (SDA) dermatophyte test medium (DTM) and dermatophyte identification medium (DIM) were compared as previously described by El-Gendy (2010) and El-Gendy et al. (2014).

Production of virulence factors by dermatophytic fungi

Both enzymatic and non enzymatic virulence factors were determined followed Achterman and White (2012), El-Gendy et al. (2014), Walailak (2015) and Elavarashi et al. (2017).

Plant samples and preparation of extracts

In this work, fresh and healthy ancient medicinal plants include the aerial parts of *P. albicans* and *T. hirsuta* as well as bulbs of *U. maritima* were collected in summer (2018) from the natural environment of Sidi-Brani city in Matrouh governorate, Egypt. Plants were washed thoroughly in tap water followed by deionized water, air-dried at room temperature and then crushed into a fine powder. 200 g of each powdered plant were extracted twice with 2000 mL of different solvents of increasing polarity (hexane, acetone and methanol) on a horizontal shaker at 37 °C and 200 rpm for 72 h. Extracts were filtered through filter paper (Whatmann No. 1), concentrated in vacuo using a rotary evaporator at 40 °C to dryness and stored in dark at 4 °C. The concentrated extracts were dissolved in DMSO to obtain a stock solution (the ratio of DMSO in the experiment did not exceed 0.5%) and stored at 4 °C (Elghuol et al. 2016).

Biochemical properties

The total polyphenol content was measured according to Medoua et al. (2009); absorbance was detected at 725 nm that expressed in gallic acid equivalents using gallic acid standard curve. Condensed tannins were estimated using the modified vanillin HCl method (Sefi et al. 2010 and Julkunen-Titto 1985), the absorbance was done at 500 nm that expressed as milligram catechin equivalents (mg CE/g DW). Total flavonoids of plant extracts were spectrophotometrically measured by the aluminum chloride colorimetric method as described by Chang *et al.* (2002). The absorbance was detected at 415 nm and expressed as mg of quercetin equivalents (QE)/g of the dry extracts. Carotenoid content was done using the method of Kurilich and Juvik (1999); absorbance was measured at 450 nm using β -carotene as standard. Total saponin contents were estimated by gravimetric method (Kaur et al. 2015). Total alkaloids were estimated as described by Biradar and Rachetti (2013). All samples were analyzed in triplicate.

Inoculum preparation and agar diffusion method for anti-dermatophytes assay

Dermatophytic strains were cultured in Sabouraud dextrose broth at 28 °C for two weeks till the highest numbers of conidia maintained. Conidia for analysis were collected after centrifuging at 4 °C, suspending in sterilized distilled water and adjusting to 10^5 conidia per ml. 100 μ L of each fungal suspension were spread on SDA medium. Different concentrations of extracts 50, 100 and 200 μ g of each extract were prepared in dimethyl sulfoxide (DMSO) and each extract concentration (10 μ L) was applied to discs of Whatman paper (No.1) and applied into SDA medium inoculated by a fungal inoculum to evaluate the antimycotic activity of each extract of each plant by the disc diffusion technique. Fungal toxicity was expressed in terms of percentage of mycelial growth inhibition and measured consistent with the formula of Pandey et al. (1982): $(dc-dt)/dc \times 100$, where dc = average diameter of fungal colony with control and dt = average diameter of fungal colony with treatment. Agar plates with 1% of DMSO and 100 μ g of clotrimazole were involved as negative and positive controls.

In vitro antiproliferative activity assay

Antiproliferative activities of plant extracts at various concentrations ranged between 25 and 300 μ g/mL against various human carcinoma cell lines including human breast adenocarcinoma (MCF-7), human cervical carcinoma (HeLa), colon cancer (HCT-116) and hepatocellular carcinoma (HepG-2) (purchased from American Type Culture Collection, ATCC, and maintained in the proper conditions) were examined and then cell viability was assessed followed the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method. The cellular viability is expressed as $(\text{sample-blank}) / (\text{control-blank}) \times 100\%$. The activity of cells in presence of test solvent only (DMSO) is considered as a control (Weichert et al. 1991; El-Gendy et al. 2018b).

Results And Discussion

Isolation and enumeration of dermatophytic fungi

Among 300 specimens scanned; 222 (74.00%), 234 (78.00%) and 279 (93.00%) of total samples showed positive results for the evidence of fungal elements by direct microscopic (KOH⁺), SDA and RSM culture methods, respectively while 78 (26.00%), 66 (22.00%), and 21 (7.00%) of total samples show no evidence of the fungi with these methods, respectively (Table 1). The culture method was better than microscopic method because of KOH preparation not only produce carbonate crystals by adsorbing CO₂ but also form fat pellets in the slide after heating slightly, hence decreasing efficacious visualization of fungi (Rebell and Taplin 1970; El-Gendy 2010; El-Bondkly et al. 2012; El-Gendy et al. 2014).

Concerning to the correlation between direct microscopic examination and culture method on SDA or RSM medium, 183 (61.00%) isolates were positive for presence of fungi in both KOH and SDA medium tests. Moreover, 51 (17.00%), 21 (7.00%) and 45 (15.00%) of samples gave negative results with microscopic, culture method on SDA medium and both methods, respectively while by applying both direct microscopic test and culture method on RSM together, 210 (70.00%) and 9 (3.00%) of samples gave positive and negative results, respectively for fungal elements. Thus, these results support RSM adequacy as a direct isolation method for clinical dermatophytic fungi than SDA specifically, it is appropriate for phenotypic characterization. Likewise, the isolation frequency of fungi on SDA (n=234, 78.00%), was less than RSM (n=279, 93.00%) because of RSM medium containing different antibiotics that provide a differentiating quality medium for isolating dermatophytes and inhibited non-dermatophytes (El-Gendy 2010; El-Bondkly et al. 2012; El-Gendy et al. 2014). As stated by Madhavi et al. (2011) 33% of total samples showed no fungal element on both direct microscopic and culture methods but 43 and 58% of the samples were distinguished using direct microscopic and culture method, respectively.

Specification and validation of dermatophytic differentiation media

Based on phenotypic and chemotypic characteristics, 253 isolates (90.68%) of 279 isolates obtained after culturing on RSM were actual dermatophytic fungi. While 45 dermatophytic fungi were unable to alter the RSM medium coloration, 19 non dermatophytic fungi; 11 *Candida* sp.; 1 spore-forming bacterium of *Bacillus* sp.; 1 Gram negative strain of *Escherichia coli* and 2 Gram positive isolates of *Staphylococcus aureus* were able to change RSM medium color (Table 2).

Moreover, our data proved that DTM medium is not completely specified for dermatophytes because of 11, 9, 4, 2, and 2 non-dermatophytic fungi, *Candida* sp., spore-forming bacilli, *S. aureus* and *Escherichia coli* respectively were able to grow and change DTM medium color but 33 dermatophytic isolates were unable to change the color of DTM. Many non-dermatophytic fungi have culture morphology like that of dermatophytes routinely isolated from clinical samplings and they are able to change DTM color which can be attributed to these fungi have resistance to the concentration of antifungal antibiotic applied in DTM and thus leading to false positive dermatophytes results (El-Bondkly et al. 2012; El-Gendy et al. 2014). These finding suggested that RSM and DTM media failed to be the preferred medium for fast differentiation of true dermatophytic fungi among clinical isolates and reflect the argement demand another confirmatory and selective medium. In this regard the ability of DIM medium to eliminate untruthful positive results obtained with commercial market media like RSM and DTM was evaluated. All dermatophytic isolates (n=253) recovered from RSM were capable of growing on DIM as well as turning its color to dark purple after 96 h of incubation (Table 2). Moreover, 6 isolates of non-dermatophytic fungi and 3 *Candida* species grown in DIM without altering its color while one isolate belong to *Candida* changed the color of DIM medium. The positive color change result of *Candida* strain on DIM medium can be rule out depending on it was much less intense those produced by different dermatophytic species the growth of *Candida* as creamy bacteria like colonies easy distinguishing from dermatophytes. Hence, when we take these two criteria into consideration, DIM medium specificity and sensitivity for dermatophytic fungi can be rose from 99.61% to 100%. Effectiveness and validation of DIM toward eliminating problems of untruthful positive results occurred with RSM and DTM media owing to its higher content of cycloheximide, 4 mg/mL, and incubation at 37 °C in comparison to 0.5 mg/mL and 30 °C in DTM as previously reported by Gromadzki et al. (2003), El-Gendy (2010), El-Bondkly et al. (2012) and El-Gendy et al. (2014).

Evaluation of different virulent factors in dermatophytes

Dermatophytes secrete many enzymes to hydrolyze the host tissue components as a source of nutrients. Moreover, released enzymes act as antigens and stimulate different degrees of inflammation. Interestingly all endophytic genera and species in this evaluation were potent enzymatic and non enzymatic virulent factors producers, which reflect the high pathogenicity of these isolates (Table 3). High keratinase activity was determined in *M. cookie*, *E. floccosum*, *T. rubrum* and *Trichophyton vaoudei* (23.56, 22.08 20.35 and 20.14 U/mL, respectively) on stratum corneum followed by (21.62, 19.07, 18.3 and 17.41 U/mL, respectively) on human hair and (22.10, 17.90, 16.00 and 15.88 U/mL, respectively) on human nail but the maximum yield of protease activity estimated in *T. rubrum*, *M. ferrogenium*, *T. tonsurance*, *M. canis* (29.91, 28.63, 27.59 and 26.91 U/mL, respectively) on stratum corneum followed by (28.00, 25.31, 27.45 and 25.09 U/mL, respectively) on human hair or (29.54, 28.11, 27.00 and 25.41 U/mL, respectively) on human nail. Moreover, stratum corneum was the best substrate for the induction of phospholipase in fungal strains *M. persicolor*, *M. racemosum*, *M. ferrogenium*, *T. erinacei* and *T. mentagrophytes* (62.25, 60.34, 60.11, 57.37 and 54.55, U/mL, respectively). Hewitt and Vincent (1989) and El-Gendy et al. (2010, 2014) in terms of the capability of dermatophytes to parasitize the host relies on the function of keratinase, protease, phospholipase, lipase, etc... not only for elastin, keratin, collagen and phospholipids degradation to provide substrates to fungi but also to stimulate delayed hypersensitivity.

On the other hand, all human substrates supported the melanoid pigment formation as one of the most active non enzymatic virulence factor by these dermatophytic fungi under study but the highest amounts of melanin were formed by *E. floccosum*, *T. rubrum*, *M. gallinae*, *T. tonsurance*, *T. erinacei* and *M. gypseum* (0.772, 0.771, 0.762, 0.704, 0.697 and 0.683, mg/mL, respectively) on human nail as the best inducer for melanin formation. Consequently, understanding the specific virulence factors responsible for pathogenicity of dermatophytes will help develop new therapeutic strategies. Our data are in line with El-Gendy et al. (2014) who stated that dermatophytic fungi synthesize a wide range of enzymatic virulence factors for instance keratinases, proteases and phospholipases upon different substrate specificities as well as non enzymatic factors like melanoid pigments, which are involved in the adherence process and pathogenicity of dermatophytes.

Evaluation the antifungal activity of different plant extracts against dermatophytes

In Table (4) we reported that hexane extract of all plants under study exhibited the lowest inhibitory activity percentage against all dermatophytic fungi obtained in this work but the maximum activity was noticed with methanol and acetone extracts, thus there is compatibility between the polarity of both solvent and antifungal metabolites and their solubility is effective in methanol or acetone but not in hexane (El-Gendy 2010).

Growth of *M. audouinii*, *M. canis*, *T. soudanense*, *T. erinacei*, *M. persicolor*, *M. gypseum*, *M. ferrogenium*, *M. cookie*, *M. gallinae* and *M. racemosum* isolates totally repressed by the methanolic extract of *P. albicans* at concentrations of 100 and 200 µg/mL but *T. vaoudei* isolate at 200 µg/mL. Moreover, the methanolic extract of *P. albicans* at concentrations of 50, 100 and 200 µg/mL gave the lowest growth inhibition activity toward the growth of *E. floccosum* (9.3 ± 0.1%, 30.0 ± 0.3% and 33.0 ± 0.7%) followed by *T. rubrum* (33.3 ± 0.0%, 56.7 ± 0.0% and 80.0 ± 0.0%), *T. tonsurance* (11.8 ± 0.7%, 66.0 ± 0.9% and 88.0 ± 0.0%) and *T. mentagrophytes* (56.7 ± 0.4%, 80.0 ± 0.0% and 93.0 ± 0.0%), respectively. Furthermore, the acetone extract of *P. albicans* gave similar results to the methanol extract except for *T. soudanense* and *T. rubrum* strains due to both of them were totally inhibited at 200 µg/mL of acetone extract. From data in Table (4) the *P. albicans* have potent anti-dermatophytic activity against all *Microsporum* species (100% of isolates were inhibited) followed by *Trichophyton* species (50% and 66.67% of isolates were inhibited by methanol and acetone extracts, respectively) with poor activity against *E. floccosum*. Sepahvand et al. (2018) and El-Demerdash (2018) reported these medicinal plants extracts as the most effective medicinal plants for dermatophytosis in development of plant-based medicines against fungi due to their potent fungitoxic properties.

Furthermore, whereas the highest reducing power against the growth of *Trichophyton* and *Epidermophyton* species was achieved after treatment with the methanolic extract of the ancient Egyptian medical plant *T. hirsuta*. The growth of all *Trichophyton* species (*T. soudanense*, *T. erinacei*, *T. rubrum*, *T. tonsurance*, *T. vaoudei* and *T. mentagrophytes*) and *E. floccosum* was 100% inhibited by the methanolic extract of *T. hirsuta* at concentrations of 100 and 200 µg/mL as well as acetone extract at 100 µg/mL. growth of *M. audouinii*, *M. gypseum*, *M. ferrogenium*, *M. cookie*, *M. canis*, *M. persicolor*, *M. gallinae*, *M. racemosum* isolates was inhibited by (28.3 ± 0.5% and 40.7 ± 0.0%), (80.0 ± 2.0% and 90.0 ± 0.0%), (29.3 ± 0.4% and 50.0 ± 0.0%), (50.0 ± 1.2% and 67.0 ± 0.0%), (70.0 ± 1.3% and 83.0 ± 0.0%), (80.0 ± 0.4% and 88.0 ± 2.4%), (42.0 ± 2.1% and 45.0 ± 1.9%) and (28.3 ± 0.1% and 46.0 ± 2.5%) after treatment with methanol and acetone extracts individually at a concentration of 200 µg/mL, respectively (Table 4). Egyptian medical plant *T. hirsuta* extracts were reported to have

antimicrobial, antitumor, antihypoglycemic and antioxidant activities due to their high phenolic compound contents (Yahyaoui et al. 2017). Study of Felhi et al. (2017) proved that extracted aerial parts of *T. hirsuta* exhibited a moderate to strong antimicrobial action against yeasts and bacteria. Abed et al. (2014) reported that among hexane, acetone and methanolic extracts of *T. hirsuta*, methanolic extract was the most active toward bacteria with inhibition zones equal to 11 to 25 mm in diameter which refer to the presence of biologically active metabolites of different chemical types in its MeOH extract for instance phenolic compounds.

Data in Table (4) showed that no growth was detected for *T. rubrum*, *T. tonsurans*, *T. erinacei*, *M. audouinii*, *M. gypseum*, *M. cookei*, *M. persicolor*, *M. gallinae* and *E. floccosum* isolates with 50, 100 and 200 µg/mL of *U. maritima* extracted with methanol or acetone which is much lesser than that of the *P. albicans* and *T. hirsuta* extracts that might be indicates the existence of broad spectrum metabolic inhibitors in *U. maritima* extracts against pathogenic fungi. Furthermore, with increasing concentrations to 100 or 200 µg/mL of both extracts individually each of *T. mentagrophytes*, *T. soudanense*, *T. vaoudei*, *M. ferrogenium*, *M. canis* and *M. racemosum* strains failed to grow. Aboelsoud (2010) and El-Demerdash (2018) reported that *U. maritima* is one of the best leading therapeutic plants in ancient Egypt. Antibacterial activity of *U. maritima* methanolic extract against various pathogens showed different antimicrobial properties of plant extracts. *B. cereus* ATCC10876 was the most inhibited pathogen with adiameter of inhibition zone 11 mm, followed by *Acinetobacter baumannii* (10 mm) and *Salmonella typhimurium* (9 mm) and this activity attributed to the presence of secoiridoid, glucosides, phenylethanoids and flavonoids contained in the extract (Belhaddad et al. 2017). The potent inhibitory activity of these plants against dermatophytic fungi is important because these fungi are the main reason of death and infectious diseases globally each year.

Determination of the antitumor activity of different plant extracts against human cancer cell lines

A dose-dependent inhibition in cells viability after treating with each extract for each plant as illustrated in Figures 1, 2, and 3. The methanolic extract of *P. albicans* reduce the viability of HCT-116, HepG-2, MCF-7 and HeLa cell lines to (41%, 40%, 80% and 81%); (30%, 20%, 66% and 70%); (19%, 0%, 49% and 57%); (5%, 0%, 35% and 45%) and (0, 0, 21, and 40%) compared to (47, 50, 88, and 89%); (33, 30, 79 and 80%); (22, 0, 60, and 70%); (16%, 0%, 40% and 59%) and (0%, 0%, 36% and 50%) with acetone extract of *P. albicans* at dosage of 25, 50, 100, 200 and 300 µg/mL, respectively. Similar to our results Nazarizadeh et al. (2013) reported that *P. major* methanol extract (1 µg/mL) was cytotoxic against cervix and ovary carcinoma with stimulating the proliferation of nasopharynx carcinoma along with other activities like wound healing, anti-inflammatory, anti-fatigue and hematopoietic. Interestingly, Gálvez et al. (2003) evaluated the cytotoxic activity of *Plantago* species against MCF-7 and UACC-62 cells and the strong cytotoxicities were detected in methanolic extracts of *Plantago coronopus* and *Plantago bellardii* with IC₅₀ equal to 32 and 34 µg/mL against MCF-7 and UACC-62, respectively.

However, death in HCT-116, HepG-2, MCF-7, and HeLa carcinoma cell lines equal to (10%, 20%, 23% and 60%); (16%, 40%, 58% and 80%); (40%, 50%, 80% and 100%); (51%, 65%, 100% and 100%) and (49%, 82%, 100% and 100%) was reported after treatment with methanol extract of *T. hirsuta* but with acetone extract it has been estimated to be (20%, 26%, 15% and 53%); (25%, 50%, 31% and 70%); (33%, 60%, 60% and 89%); (60%, 71%, 81% and 100%) and (67%, 89%, 97% and 100%) at a concentrations of 25, 50, 100, 200, and 300 µg/mL, respectively (Fig. 2). HCT-116 showed the highest resistant to *T. hirsuta* but while HeLa followed by MCF-7 cell line showed the highest sensitivity for both methanolic and acetone extracts of *T. hirsuta*. Previously, polar extracts of *T. hirsuta* exhibited dose dependent cytotoxic effect on human colon cancer cell growth (Akrouit et al. 2011) and HeLa cell viability with IC₅₀ value 175 µg/mL (Felhi et al. 2017).

Overall, *U. maritima* methanolic extract exhibited the highest cytotoxicity against HCT-116 followed by MCF-7 and HepG-2 cell lines but the lowest activity was recorded with cervical cancer. The viability of HCT-116, MCF-7 and HepG-2 cell lines was totally repressed with 100 µg/mL (TGI~100 µg/mL) whereas the growth of HeLa cell line was reduced to 10% at 100 µg/mL of *U. maritima* methanolic extract and totally killed at 200 µg/mL. On the other hand, HCT-116 and MCF-7 cancer cell lines failed to survive at 100 µg/mL of *U. maritima* acetone extract but HeLa and HepG-2 cell lines killed by 200 and 300 µg/mL of acetone extract, respectively. *Urginea maritima* is endemic to Egypt, well known for its traditional medicine applications and it is typical for treating malignancies by reason of their selective killing of cancer cell by apoptosis instead of necrosis. *Urginea maritima* selectively repressed the proliferation of SH-SY5Y malignant cells in dose-dependent mode (Elghuol et al. 2016). Al-Dabbagh et al. (2019) noticed the same observations in HepG-2 cells treated with the ethanolic extract of *Matricaria recutita* L. with IC₅₀ ~300 µg/mL. Mohamed et al. (2014) isolated urgeineglyceride A and quercetin-3'-O-β-d-glucopyranoside from *U. maritima* extract with repression activity toward lung, glioblastoma and prostate cancer cell lines. Then these plants, *P. albicans*, *T. hirsuta* and *U. maritima* appear to be among the preferred drugs in the future to treat these deadly diseases.

Phytochemical analysis of selected plant extracts

All the investigated Egyptian medical plants exhibited an amazing presence of significant phytochemicals that involved in several biological activities and the quantities of secondary metabolites were increased through increasing the polarity of solvents used, so the maximum yields were detected in methanol extract followed by acetone while the lowest amount was detected in hexane extract (Table 5). These results highlighting the chemical differences between various extracts of each plant obtained in accordance with solvent. Yahyaoui et al. (2017, 2018a, b) reported that the content of polyphenols, flavonoids tanins, alkaloids and other phytochemicals are varying considerably according to the solvents used, polarity of solvent, extraction methods, particle size and geographical origin. The phytochemical investigations of *P. albicans* revealed the presence of various chemical constituents of great clinical importance with a history of pharmacological effects, i.e. polyphenols (31.25 ± 0.011, 100.61 ± 0.010 and 100.58 ± 0.018 mg/g); flavonoids (25.00 ± 0.18, 53.19 ± 0.40 and 50.92 ± 0.39 mg/g); condensed tannins (1.22 ± 0.00, 7.80 ± 0.30 and 6.71 ± 0.18 mg/mL); carotenoids (0.43 ± 0.20, 2.99 ± 0.15 and 2.46 ± 0.12 mg/mL); lutein (0.25 ± 0.01, 0.85 ± 0.05 and 0.76 ± 0.04 mg/mL), crude saponins (1.0 ± 0.05%, 1.90 ± 0.09% and 1.80 ± 0.09%) and alkaloids (0.00 ± 0.00%, 0.50 ± 0.00% and 0.44 ± 0.00%) in hexane, methanol and acetone extracts, respectively. These data are in line with Francoise et al. (2008) investigation of *Plantago* species phytochemicals which revealed the occurrence of various chemical ingredients, i.e. steroids, tannins, coumarins, lipids, flavonoids, iridoids, polysaccharides, sterols and volatile substances of medication importance.

Phytochemical composition of *T. hirsuta* was total polyphenols (48.15 ± 0.01 , 150.09 ± 0.05 and 142.16 ± 0.01 mg/g); total flavonoids (15.76 ± 1.65 , 41.83 ± 0.31 and 40.39 ± 0.26 mg/g); condensed tannins (2.31 ± 0.05 , 9.00 ± 0.22 and 7.63 ± 0.19 mg/mL); carotenoids (0.32 ± 0.05 , 3.53 ± 0.10 and 3.04 ± 0.14 mg/mL); lutein (0.03 ± 0.01 , 0.17 ± 0.01 and 0.17 ± 0.02 mg/mL); crude saponins ($1.2 \pm 0.04\%$, $2.4 \pm 0.05\%$ and $2.4 \pm 0.05\%$) and alkaloids ($0.32 \pm 0.00\%$, $1.70 \pm 0.04\%$ and $1.58 \pm 0.04\%$) in hexane, methanol and acetone extracts, respectively. Our data are in harmony with Yahyaoui et al. (2017) with a view to the methanolic extracts of *T. hirsuta* aerial parts in their study gave the high amount of flavonoids ranged from 88.76 ± 7.24 to 163.64 ± 3.32 mg QE/gdw, followed by hexane extract (30.45 ± 2.15 to 37.26 ± 0.51 mg QE/gdw). Phytochemical composition of the aerial part of *T. hirsuta* methanolic extract performed by Yahyaoui et al. (2018a, b) possessed the highest total phenol contents (191.59 ± 2.09 to 362.74 ± 3.49 mg EAG/gdw) followed by the hexane (53.81 ± 2.19 to 165.47 ± 4.95 mg EAG/gdw) and Abed et al. (2014) who reported that the amount of condensed tannins in the methanolic extract of *T. hirsuta* ranged between 9.45 ± 1.22 and 0.09 ± 0.02 mg EAG/gdw.

The secondary metabolites of *U. maritima* were composed of total polyphenols (23.92 ± 0.021 , 362.74 ± 3.49 and 329.58 ± 0.05 mg/g); total flavonoids (17.63 ± 0.41 , 65.30 ± 0.51 and 45.24 ± 0.50 mg/g); condensed tannins (5.13 ± 0.11 , 13.96 ± 0.20 and 9.96 ± 0.22 mg/mL); total carotenoids (2.93 ± 0.15 , 5.84 ± 0.13 and 3.21 ± 0.18 mg/mL); lutein (0.18 ± 0.01 , 0.61 ± 0.05 and 0.43 ± 0.04 mg/mL); crude saponins ($0.8 \pm 0.05\%$, $2.35 \pm 0.10\%$ and $1.22 \pm 0.07\%$) and alkaloids ($0.1 \pm 0.01\%$, $1.87 \pm 0.09\%$ and $1.39 \pm 0.06\%$) in hexane; methanol and acetone extracts, respectively. Our data are consistent with Belhadda et al. (2017) who recommended that the bulb of *U. maritima* methanolic extract contained the highest level of flavonoid, glycoside, tannin, anthraquinone, anthocyanin, triterpenoids, steroid and reducing compounds. Phenolic compounds are associated with a broad spectrum of pharmacological and health promoting effects and they are important essential constituent in a diverse nutraceutical, therapeutical and cosmetic applications (Elghuol et al. 2016). Tannins have been found to have antiviral, antibacterial, anti-parasitic, anti-inflammatory, antiulcer and antioxidant effects for possible therapeutic applications (Elghuol et al. 2016). Therefore, the concentration of these compounds could contribute synergistically to the significant pharmacological actions (Al-Dabbagh et al. 2019).

Conclusions

In conclusion, all data approve the significance of Egyptian ethnomedical plants as potent source of diverse bioactive pharmaceutical metabolites. The efficiency of *P. albicans*, *T. hirsuta* and *U. maritima* against cancer and invasive fungi could confirm their place in medication with a massive economic and health advantage universal. Accordingly, further studies regarding isolation and purification of active phyto-constituents with broad spectrum of antioxidant and antibacterial activities are under investigation.

Declarations

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Authors' contributions

EAM El-Bondkly, MMAA El-Gendy, AAM El-Bondkly, FS El-Shenawy and AAM El-Bondkly, designed and carried out the work, accomplished literature searches, analyzed data and wrote the manuscript. All the authors read and approved the final manuscript.

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Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Abid S, Lekchir A, Mekhf H, Zlyyat A, Legssyer A, Aziz M, Bnouham M (2014) Inhibition of α -glucosidase and glucose intestinal absorption by *Thymelaea hirsuta* fractions. J Diabetes 6:351-359. doi: 10.1111/1753-0407.12106
2. Aboelsoud NH (2010) Herbal medicine in ancient Egypt. J Med Plant Res 4(2):082-086
3. Achterman RR, White TC (2012) Dermatophyte virulence factors: Identifying and analyzing genes that may contribute to chronic or acute skin infections. Int J Microbiol Article ID 358305. doi: 10.1155/2012/358305
4. Akrouit A, Gonzalez LA, El Jani HM, Madrid PC (2011) Antioxidant and antitumor activities of *Artemisia campestris* and *Thymelaea hirsuta* from southern Tunisia. Food Chem Toxicol 49:342-347. doi: 10.1016/j.fct.2010.11.003
5. Al-Dabbagh B, Elhaty IA, Elhaw M, Murali C, Al Mansoori A, Awad B, Amin A (2019) Antioxidant and anticancer activities of chamomile (*Matricaria recutita* L.). BMC Res Notes 12:3. doi: 10.1186/s13104-018-3960-y
6. Alves-Silva JM, Romane A, Efferth T, Salgueiro L (2017) North African medicinal plants traditionally used in cancer therapy. Front Pharmacol 8:383. doi: 10.3389/fphar.2017.00383
7. Belhaddad OE, Noureddine C, Amamra S, Zerargui F, Baghiani A, Khennouf S, Arrar L (2017) Chromatographic fractionation, antioxidant and antibacterial activities of *Urginea maritima* methanolic extract. Pak J Pharm Sci 30:127-134
8. Biradar SR, Rachetti BD (2013) Extraction of some secondary metabolites and thin layer chromatography from different parts of *Centella asiatica* L. (URB). American J Life Sci 1:243-247. doi: 10.11648/j.ajls.20130106.11
9. Chang CC, Yang MH, Wen HM, Chern JC (2002) Estimation of total flavonoid content in propolis by two complementary colorimetric methods. J Food Drug Anal 10:178-182. doi: 10.12691/jnh-5-2-4
10. Elavarashi E, Kindo AJ, Rangarajan S (2017) Enzymatic and nonenzymatic virulence activities of dermatophytes on solid media. J Clin Diagn Res 11:DC23-DC25. doi: 10.7860/JCDR/2017/23147.9410
11. El-Bondkly AMA, El-Gendy MMA, Bassyouni RH (2012) Overproduction and biological activity of prodigiosin-like pigments from recombinant fusant of endophytic marine *Streptomyces* species. Antonie van Leeuwenhoek 102:719-734. doi: 10.1007/s10482-012-9772-5
12. El-Demerdash M (2018) Medicinal plants of Egypt. In: Saxena PK (Ed) Development of plant-based medicines, Studies in Mycology 89:153-175
13. El-Gendy MMA (2010) In vitro, evaluation of medicinal activity of Egyptian honey from different floral sources as anticancer and antimycotic infective agents. J Microbial Biochem Technol 2:118-123. doi:10.4172/1948-5948.1000035
14. El-Gendy MMA, El-Bondkly AMA, Yahya SMM (2014) Production and evaluation of antimycotic and antihepatitis C virus potential of fusant MERV6270 derived from mangrove endophytic fungi using novel substrates of agroindustrial wastes. Appl Biochem Biotechnol 174:2674-2701. doi: 10.1007/s12010-014-1218-2
15. El-Gendy MMA, Al-Zahrani SH, El-Bondkly AMA (2017) Construction of potent recombinant strain through intergeneric protoplast fusion in endophytic fungi for anticancerous enzymes production using rice straw. Appl Biochem Biotechnol 183:30-50. doi: 10.1007/s12010-017-2429-0
16. El-Gendy MMA, Yahya SMM, Hamed AR, Soltan MM, El-Bondkly AMA (2018a) Phylogenetic analysis and biological evaluation of marine endophytic fungi derived from Red Sea sponge *Hyrtios erectus*. Appl Biochem Biotechnol 185:755-777. doi: 10.1007/s12010-017-2679-x
17. El-Gendy MMA, Mohamed Z, Hekal N, Ali F, Yousef A (2018b) Production of bioactive metabolites from different marine endophytic *Streptomyces* species and testing them against methicillin-resistant *Staphylococcus aureus* (MRSA) and cancer cell lines. BioTechnologia 99:13-35. doi: 10.5114/bta.2018.73559
18. Elghuol MM, Abdul KK, Zain MM, Said MSM (2016) Apoptosis inducer capacity of cardiotonic steroids of *Urginea maritima* extract on SH-SY5Y neuroblastoma cells, with less susceptibility among neuron-module cells. American J Appl Sci 13:686-696. doi: 10.3844/ajassp.2016.686.696
19. Felhi S, Chaaibia M, Bakari S, Ben Mansour R, Békir A, Gharsallah N, Kadri A (2017) Anti-microbial screening and cytotoxic activity of aerial part of *Thymelaea hirsuta* L. essential oil growing in south-west Tunisia. Pak J Pharm Sci 30:087-091
20. Françoise F, Annick G, Sylvie R (2008) Culture of *Plantago* species as bioactive components resources: a 20-year review and recent applications. Acta Botanica Gallica 155:277-300. doi: 10.1080/12538078.2008.10516109
21. Gálvez M, Martí C, Cordero N, López-Lázaro M, Cortés F, Ayuso J (2003) Cytotoxic effect of *Plantago* Spp. on cancer cell lines. J Ethnopharm 88:125-130
22. Gromadzki S, Ramani R, Chaturvedi V (2003) Evaluation of new medium for identification of dermatophytes and primary dimorphic pathogens. J Clin Microbiol 41:467-468. doi: 10.1128/JCM.41.1.467-468.2003
23. Hewitt W, Vincent S (1989) Theory and application of microbiological assay. New York, Academic Press pp. 38-79
24. Ibrahim AS, Khaled HM, Mikhail NH, Baraka H, Kamel H (2014) Cancer incidence in Egypt: Results of the National Population-Based Cancer Registry Program. J Cancer Epidemiol Article ID 437971. doi: 10.1155/2014/437971
25. Julkunen-Titto R (1985) Phenolic constituents in the leaves of northern willows: methods for the analysis of certain phenolics. J Agric Food Chem 33:213-217. doi: 10.1021/jf00062a013
26. Kane J, Summerbell R, Sigler L, et al (1997) Laboratory handbook of dermatophytes. Belmont, Star Publishing Co.
27. Kaur R, Arora S, Thukral AK (2015) Quantitative and qualitative analysis of saponins in different plant parts of *Chlorophytum borivialum*. Int J Pharm Bio Sci 6:826-835
28. Koneman EW (2006) Color atlas and text book of diagnostic microbiology. Lippincott Williams and Wilkins 6:1187
29. Kurilich A, Juvik J (1999) Quantification of carotenoid and tocopherol antioxidants in *Zea mays*. J Agric Food Chem 47:1948-1955
30. Larone DH (2002) Medically important fungi: A guide to identification (4th ed.), Washington, D.C., American Society for Microbiology Press

31. Madhavi S, Rama RMV, Jyothsna K (2011) Mycological study of dermatophytosis in rural population. *Annals Biol Res* 2:88-93
32. Medoua GM, Egal AA, Oldewage-Theron WH (2009) Nutritional value and antioxidant capacity of lunch meals consumed by elderly people of Sharpeville, South Africa. *Food Chem* 115:260-264. doi: [10.1016/j.foodchem.2008.12.007](https://doi.org/10.1016/j.foodchem.2008.12.007)
33. Merz WG, Roberts GD (1995) In Murray PE, Baron EJ, Pfaller MA, Tenover FC, Tenover RH (Eds), *Manual of clinical microbiology* (6th ed. pp. 709-722) Washington: ASM Press
34. Metiner K, Özkan O, Ak S (2012) Antibacterial effects of ethanol and acetone extract of *Plantago major* L. on gram positive and gram negative bacteria. *Kafkas Univ Vet Fak Derg* 18:503-505. doi: [10.9775/kvfd.2011.5824](https://doi.org/10.9775/kvfd.2011.5824)
35. Mohamed GA, Shaala LA, Youssef D, Ibrahim Sabrin RM, Alshali KZ (2014) Urgineaglyceride A: A new monoacylglycerol from the Egyptian *Drimys* *maritima* bulbs. *Nat Prod Res* 28:1583-1590. doi: [10.1080/14786419.2014.927468](https://doi.org/10.1080/14786419.2014.927468)
36. Nazarizadeh A, Mikaili P, Moloudizargari M, Aghajanshakeri S, Javaherypour S (2013) Therapeutic uses and pharmacological properties of *Plantago major* L. and its active constituents. *J Basic Appl Sci Res* 3:212-221
37. Nofal ZA, El-Maghraby AF, Gad MR, Farghaly AA, Attia EMA (2016) Evaluation of the protective effect of ethanolic extract of *Plantago major* plant against CCl₄ induced genotoxicity and biochemical disturbance in Rat. *Egypt J Vet Sci* 47:83-110
38. Pandey DK, Tripathi NN, Tripathi RD, Dixit SN (1982) Fungitoxic and phytotoxic properties of the essential oil of *Hyptis suaveolens*. *J Plant Dis Prot* 89:344-349
39. Rebell G, Taplin D (1970) *Dermatophytes, their recognition and identification*. 2nd (Ed) Miami University Press, Miami
40. Rinaldi MG, Stevens VJ, Halde C (1973) A New sporulation medium for primary isolation and identification of dermatophytes. Abs: AmerSoc Micro Meeting Miami
41. Sefi M, Fetoui H, Makni M, Zeghal N (2010) Mitigating effects of antioxidant properties of *Artemisia campestris* leaf extract on hyperlipidemia, advanced glycation end products and oxidative stress in alloxan-induced diabetic rats. *Food Chem Toxicol* 48:1986-1993. doi: [10.1016/j.fct.2010.05.005](https://doi.org/10.1016/j.fct.2010.05.005)
42. Sepahvand A, Eliasy H, Mohammadi M, Safarzadeh A, Azarbaijani K, Shahsavari S, Alizadeh M, Beyranvand F (2018) A review of the most effective medicinal plants for dermatophytosis in traditional medicine. *Biomed Res Therapy* 5:2378-2388. doi: [10.15419/bmrat.v5i6.450](https://doi.org/10.15419/bmrat.v5i6.450)
43. Van TC, Ngoc KHT, Van TN, Hau KT, Marco G, Satolli F, Feliciani C, Tirant M, Vojvodic A, Lotti T (2019) Antifungal susceptibility of dermatophytes isolated from cutaneous fungal infections. The Vietnamese Experience Open Access Maced J Med Sci 7:247-249. doi: [10.3889/oamjms.2019.062](https://doi.org/10.3889/oamjms.2019.062)
44. Walailak C (2015) Virulence factors involved in pathogenicity of dermatophytes. *Dutsadee J Sci Tech* 12:573-580
45. Weichert H, Blechschmidt I, Schröder S, Ambrosius H (1991) The MTT-assay as a rapid test for cell proliferation and cell killing: application to human peripheral blood lymphocytes (PBL). *Allerg Immunol* 37:139-144
46. Yahyaoui M, Ghazouani N, Sifaoui I, Abderrabba M (2017) Comparison of the effect of various extraction methods on the phytochemical composition and antioxidant activity of *Thymelaea hirsuta* L. aerial parts in Tunisia. *Biosci Biotech Res Asia* 14:997-1007
47. Yahyaoui M, Bouajila J, Cazaux S, Abderrabba M (2018a) The impact of regional locality on chemical composition, antioxidant and biological activities of *Thymelaea hirsuta* L. extracts. *Phytomedicine* 41:13-23. doi: [10.1016/j.phymed.2018.01.010](https://doi.org/10.1016/j.phymed.2018.01.010)
48. Yahyaoui M, Ghazouani N, Saoudi S, Sifaoui I, Chammem N, Abderrabba M (2018b) Experimental design methodology application in the optimization of phytochemical compounds extraction and antioxidant activity of *Thymelaea hirsuta* L. extracts. *J Mater Environ Sci* 9:1551-1561. doi: [10.26872/jmes.2018.9.5.171](https://doi.org/10.26872/jmes.2018.9.5.171)

Tables

Table 1 The correlation between direct microscopic and culture methods of clinical samples

Culture/Microscopic	KOH (+)		KOH (-)		Total	
	n	%	n	%	n	%
SDA culture (+)	183	61.00	51	17.00	234	78.00
SDA culture (-)	21	7.00	45	15.52	66	22.00
Total	204	68.00	96	32.00	300	100.00
RSM culture (+)	210	70.00	69	23.00	279	93.00
RSM culture (-)	12	4.00	9	3.00	21	7.00
Total	222	74.00	78	26.00	300	100.00

Table 2 Specificity and efficiency of various culture media for isolation of dermatophytes

Clinical fungal isolates	Growth on			Color change on		
	RSM	DTM	DIM	RSM	DTM	DIM
Dermatophytic fungi						
<i>T. rubrum</i>	41	41	41	29	33	41
<i>T. mentagrophytes</i>	40	40	40	31	36	40
<i>T. tonsurance</i>	34	34	34	29	29	34
<i>T. soudanense</i>	13	13	13	13	11	13
<i>T. vaoundei</i>	6	6	6	6	6	6
<i>T. erinacei</i>	5	5	5	3	4	5
<i>M. audouinii</i>	9	9	9	7	8	9
<i>M. gypseum</i>	14	14	14	14	11	14
<i>M. ferrogenium</i>	11	11	11	10	11	11
<i>M. cookie</i>	19	19	19	16	13	19
<i>M. canis</i>	16	16	16	13	16	16
<i>M. persicolor</i>	14	14	14	10	12	14
<i>M. gallinae</i>	7	7	7	7	7	7
<i>M. racemosum</i>	8	8	8	7	8	8
<i>E. floccosum</i>	16	16	16	13	15	16
Total non dermatophytic fungi	26	14	6	19	11	0
Total <i>Candida</i> sp.	16	10	3	11	9	1
Spore forming bacilli	5	4	0	1	4	0
<i>Staphylococcus aureus</i>	4	2	0	2	2	0
<i>Escherichia coli</i>	5	2	0	1	2	0

Table 3 Enzymatic virulence factors formation in dermatophytic fungi on different human substrates

Dermatophytic fungi	Virulence factors production											
	Stratum comeum				Human hair				Human nail			
	K	PL	P	M	K	PL	P	M	K	PL	P	M
<i>T. rubrum</i>	20.35	22.46	29.91	0.62	18.13	22.55	28.00	0.60	16.00	23.46	29.54	0.77
<i>T. mentagrophytes</i>	11.82	54.55	15.67	0.21	10.06	53.00	15.00	0.41	8.38	48.55	14.07	0.45
<i>T. tonsurance</i>	19.26	39.12	27.59	0.67	13.63	40.12	27.45	0.58	13.91	40.16	27.00	0.70
<i>T. soudanense</i>	14.98	29.44	16.19	0.15	12.62	25.49	18.15	0.48	9.49	26.36	11.44	0.43
<i>T. vaoundei</i>	20.14	36.18	24.13	0.39	17.41	29.60	21.58	0.50	15.88	34.26	18.01	0.56
<i>T. erinacei</i>	14.56	57.37	19.33	0.55	14.01	50.00	16.40	0.50	14.00	51.27	17.40	0.69
<i>M. audouinii</i>	17.09	31.26	21.02	0.31	15.00	31.16	19.30	0.45	15.60	32.00	19.30	0.59
<i>M. gypseum</i>	18.93	33.16	19.89	0.57	16.83	30.18	20.31	0.56	15.67	36.02	19.70	0.68
<i>M. ferrogenium</i>	19.29	60.11	28.63	0.37	15.64	55.10	25.31	0.40	14.96	60.00	28.11	0.50
<i>M. cookie</i>	23.56	36.18	26.01	0.29	21.62	42.88	25.01	0.34	22.10	38.60	25.00	0.56
<i>M. canis</i>	19.86	19.09	26.91	0.23	15.00	19.65	25.09	0.40	13.98	23.47	25.41	0.66
<i>M. persicolor</i>	10.52	62.25	12.90	0.32	10.71	60.72	17.67	0.39	9.00	54.79	17.67	0.57
<i>M. gallinae</i>	14.35	15.23	18.60	0.45	10.57	16.49	15.15	0.40	9.18	10.90	15.99	0.76
<i>M. racemosum</i>	9.28	60.34	14.10	0.19	5.86	56.02	10.05	0.30	7.90	60.18	13.09	0.47
<i>E. floccosum</i>	22.08	40.65	25.74	0.62	19.07	53.84	25.00	0.60	17.90	51.23	25.40	0.77

K: keratinase, PL: Phospholipase and P: Protease productivities (U/mL) as well as M: Melanin formation (mg/mL)

Table 4 Antifungal activity of different plants extracted with different organic solvents at different concentrations against clinical dermatophytes

Plant extract/ concentration (µg/mL)	Percentage of dermatophytic fungal growth inhibition (%)									
	<i>T. rubrum</i>	<i>T. tonsurans</i>	<i>T. mentagrophytes</i>	<i>T. soudanense</i>	<i>T. vaoudei</i>	<i>T. erinacei</i>	<i>M. audouinii</i>	<i>M. gypseum</i>	<i>M. ferrogeneum</i>	<i>M. coe</i>
<i>P. albicans</i>										
EtOAc ex.										
50	19.5±0.5	3.2±0.3	10.0±0.0	21.0±0.2	21.0±1.0	70.0±0.0	20.5±0.5	30.0±1.0	23.3±0.2	20.0±1.0
100	36.1±4.6	22.0±4.1	29.8±1.0	43.8±0.8	30.8±1.0	79.1±0.0	40.8±0.6	40.3±1.0	39.8±0.7	27.1±1.0
200	58.2±4.7	57.1±4.9	45.3±2.0	60.0±1.2	49.0±1.2	75.3±1.0	51.0±0.8	45.3±1.5	51.0±0.7	35.3±1.0
Methanol ex.										
50	33.3±0.0	11.8±0.7	56.7±0.4	80.7±0.8	71.0±0.6	86.7±0.4	75.0±0.0	96.7±0.0	49.0±0.2	90.0±0.0
100	56.7±0.0	66.0±0.9	80.0±0.0	100.0±0.0	93.0±0.8	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0
200	80.0±0.0	88.0±0.0	93.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0
Acetone ex.										
50	40.0±0.0	15.0±0.0	26.1±1.7	76.0±1.2	52.1±1.2	86.0±1.3	86.9±0.0	91.0±0.0	41.8±0.1	76.1±1.0
100	70.0±0.0	43.3±1.3	88.3±1.9	90.0±0.1	91.0±0.5	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0
200	100.0±0.0	85.1±0.0	89.0±2.5	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0
<i>T. hirsuta</i>										
EtOAc ex.										
50	13.3±0.9	3.3±0.2	40.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	7.3±1.0	25.0±0.2	0.0±0.0	44.0±1.0
100	56.7±5.8	15.3±0.9	70.0±0.0	0.0±0.0	0.0±0.0	25.0±2.1	28.9±2.1	46.1±2.8	0.0±0.0	60.3±1.0
200	75.0±0.0	43.3±2.9	90.0±0.0	0.0±0.0	0.0±0.0	35.0±1.9	40.0±2.5	75.0±3.0	0.0±0.0	81.0±1.0
Methanol ex.										
50	50.0±0.0	80.0±0.4	60.0±0.0	90.0±0.0	58.0±1.0	70.0±1.5	10.0±0.4	30.0±2.0	19.9±0.4	21.5±1.0
100	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	15.0±0.0	78.3±2.9	27.0±0.6	39.1±1.0
200	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	28.3±0.5	80.0±2.0	29.3±0.4	50.0±1.0
Acetone ex.										
50	35.0±0.0	12.0±0.0	43.0±8.7	47.0±2.0	61.0±2.0	59.3±0.5	18.1±0.0	59.0±0.0	13.0±0.0	36.0±1.0
100	88.3±5.9	60.0±0.0	90.0±0.3	75.8±2.2	92.0±2.0	85.0±0.0	29.4±0.0	63.0±0.0	30.0±0.0	60.0±1.0
200	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	40.7±0.0	90.0±0.0	50.0±0.0	67.0±1.0
<i>U. maritima</i>										
.EtOAc ex.										
50	0.0±0.0	6.7±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	26.7±0.0	10.8±2.0	31.0±1.0
100	20.0±0.0	6.7±0.0	0.0±0.0	12.0±1.0	0.0±0.0	20.0±0.0	0.0±0.0	46.7±0.0	19.0±2.0	50.0±1.0
200	28.3±1.1	5.0±0.0	0.0±0.0	23.6±1.0	0.0±0.0	28.3±1.1	0.0±0.0	65.0±0.0	40.3±2.1	68.3±1.0
Methanol ex.										
50	100.0±0.0	100.0±0.0	30.0±0.7	58.0±0.7	75.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	61.5±0.4	100.0±0.0
100	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0
200	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0
Acetone ex.										
50	100.0±0.0	100.0±0.0	75.8±2.2	47.0±2.0	89.0±5.2	100.0±0.0	100.0±0.0	100.0±0.0	50.7±3.1	100.0±0.0
100	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0
200	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0
DMSO 100 µL										
	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
Clotrimazole 100 µg/mL										
	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0	100.0±0.0

Table 5 Phytochemical analysis of selected plant extracts

Phytochemical composition	Plant								
	<i>P. albicans</i>			<i>T. hirsuta</i>			<i>U. maritima</i>		
	Hexane extract	Methanol extract	Acetone extract	Hexane extract	Methanol extract	Acetone extract	Hexane extract	Methanol extract	Acetone extract
Total polyphenols (mg/g)	31.25±0.01	100.61±0.01	100.58±0.02	48.15±0.01d	150.09±0.05b	142.16±0.01	23.92±0.02	362.74±3.49	329.58±0.0
	25.00±0.18	53.19±0.40	50.92±0.39	15.76±1.65c	41.83±0.31a	40.39±0.26	17.63±0.41	65.30±0.51	45.24±0.50
Total flavonoids (mg/g)	1.22±0.00	7.80±0.30	6.71±0.18	2.31±0.05	9.00±0.22	7.63±0.19	5.13±0.11	13.96±0.20	9.96±0.22
	0.43±0.20	2.99±0.15	2.46±0.12	0.32±0.05	3.53±0.10	3.04±0.14	2.93±0.15	5.84±0.13	3.21±0.18
Condensed tannins (mg/ml)	0.25±0.01	0.85±0.05	0.76±0.04	0.03±0.01	0.17±0.01	0.17±0.02	0.18±0.01	0.61±0.05	0.43±0.04
	1.00±0.05	1.90±0.09	1.80±0.09	1.20±0.04	2.40±0.05	2.40±0.05	0.80±0.05	2.35±0.10	1.22±0.07
Total carotenoids (mg/ml)	0.00±0.00	0.50±0.00	0.44±0.00	0.32±0.00	1.70±0.04	1.58±0.04	0.10±0.01	1.87±0.09	1.39±0.06
Lutein (mg/ml)									
Crude saponins (%)									
Alkaloids (%)									

Figures

Figure 1

Effect of *P. albicans* extracts against HCT-116, HepG-2, MCF-7 and HeLa carcinoma cell lines

Figure 2

Effect of *T. hirsuta* extracts against HCT-116, HepG2, MCF-7 and HeLa carcinoma cell lines

Figure 3

Effect of *U. maritima* extracts against HCT-116, HepG2, MCF-7 and HeLa carcinoma cell lines

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