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ORIGINAL PAPER

Is it possible to use the stalks of *Gossypium hirsitum* L., an important by-product of cotton cultivation, as an alternative source of bioactive components?

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Abstract

In recent years, agricultural waste materials and wild plants have become alternative raw materials for the source of bioactive components. This study included the data from antioxidant capacity (DPPH, ABTS, CUPRAC, FRAP, phosphomolybdenum, and metal chelating) and enzyme inhibitory assays (cholinesterase, tyrosinase, α-amylase, and α-glucosidase) on *Gossypium hirsutum* L. stalk extracts as well as HPLC technique. Flavonoid contents of the extracts were found to be low, while the amounts of phenolics were found as 14.38 and 13.22 μmol gallic acid equivalents (GAEs)/g dry plant (dp) in the methanolic and aqueous extracts, respectively. The extracts were determined to contain significant amounts of apigenin, quercetin, (−)-epicatechin, and protocatechuic acid. The extracts exhibited remarkable antioxidant activity almost in all tests. In addition, the methanolic and aqueous extracts showed promising inhibitory activity on α-glucosidase. Phenolics, in particular, *p*-hydroxybenzoic and benzoic acids, were found to be in correlation with the activities of the extracts. It was concluded that the stalk, which is the post-harvest field trash of the cotton cultivation, is an alternative source of bioactive molecules and can be used in pharmaceutical and food industries for its anti-diabetic and antioxidant activities.

Keywords *Gossypium hirsutum* · Stalk · By-product · Antioxidant · Enzyme inhibitory · HPLC

Introduction

Gossypium hirsutum L. is one of the most important industrial plants produced in the world. Cultivation of the transgenic variety is usually preferred, because the plant, also called 'Mexican Cotton', 'Upland', or 'American cotton' has high yield and adaptation ability to different environmental conditions [1–3]. Cotton is also cultivated in Asia and Africa. However, the cotton growing in these regions has poor yield and its adaptation to different climatic conditions is known to be low [1, 2, 4–6].

The fully matured cotton bolls are collected and then processed in factories. Here, the fibers and the seeds are separated from each other and fibers are generally used as raw material in textile industry [2]. It is estimated that the total amount of cotton fiber produced worldwide in the period of 2013–2014 is over 23 million tones [7]. The seeds obtained as a result of this process are used in various fields such as the oil and food industries [2].

While collecting the cotton bolls, the stalks are generally left in the field. Egbuta et al. [2] named this material as 'post-harvest field trash'. The stalk, which is produced in high amounts at the end of each harvesting season, has less commercial value than cotton. The reason for leaving this material in the field is that it is usually used to meet the carbon needs of the soil. In addition, it is considered that the resistance of the soil to erosion is increased by leaving them on the land [2]. The stalks are also used in the production of

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particleboard [8–10], wood adhesive [11], ethanol [12], and briquette [13]. The stalks are also known to be used in pulp industry for its high cellulose content [14].

Cotton plant is thought to be an important source of bioactive phytochemicals [15–20]. Up to now, the whole cotton plant was shown to contain monoterpenes (in the flowers and leaves) [21–24], sesquiterpenes (in the flowers, seeds, and bolls) [16, 25], triterpenes (in the leaves) [20], phenolic acids, phenolic acid analogs, flavonoids, tannins, coumarins (in the flowers, seeds, bracts, leaves, and roots) [15], fatty acids, carbohydrates, and proteins [15, 20, 26–32]. Some of these compounds have been proven to have several biological activities such as antimicrobial, anti-inflammatory, antioxidant, cytotoxic, and contraceptive [2].

As far as we know, no study is available on the chemical composition and biological activity of this material. Moreover, there is no report on the use of cotton stalks in food and pharmaceutical industries. Millions of tons of stalk are left in the field each year. This means that a significant amount of bioactive compounds available in this material is wasted each year. Since plant species contain hundreds of unique chemical substances with interesting antioxidant and enzyme inhibitory activities, interest in plant-derived natural products has been increased steadily [33–37]. The aim of this study is to investigate the enzyme inhibitory [on acetylcholinesterase (AChE), butyrylcholinesterase (BChE), tyrosinase, α-amylase, and α-glucosidase] and antioxidant activities of the ethyl acetate (EtOAc), methanol (MeOH), and water extracts of *G. hirsutum* stalks to determine whether it can be used in the treatment of Alzheimer's disease and diabetes in food and pharmaceutical industries or. In this study, it has also been investigated whether this material has skin-whitening effect and can be used in the cosmetic applications. In the study, chemical compositions of the extracts were also determined using spectrophotometric and chromatographic techniques.

Materials and methods

Plant material

Cotton (*G. hirsitum*) stalks were collected from Cakalli village, Karaisali-Adana on 13 September 2010, and authenticated by Dr. Olcay CEYLAN, who is the senior taxonomist at the Department of Biology, Mugla Sitki Kocman University (Mugla-TURKEY). The samples were deposited under the accession number of O.5102.

Extract preparation

The air-dried stalks of *G. hirsitum* were individually extracted using the method described previously [38]. Yields were found to be 0.73, 3.78, and 5.66% (w/w) for the EtOAc, MeOH, and water extracts, respectively.

Total flavonoid and phenolic assays

Quantities of the flavonoids and phenolics in the extracts were screened using the method described by Zengin et al. [38].

Reversed-phase high-performance liquid chromatography (RP-HPLC) analysis

Phenolics were quantified by RP-HPLC method as described previously [38, 39]. Twenty-three phenolic compounds were used as the standards. Details of HPLC method and chromatographic profiles of the extracts were presented in supplementary file.

Antioxidant activity

Antioxidant activities of *G. hirsutum* stalk extracts were investigated using metal chelating, reducing power [Cupric Reducing Antioxidant Capacity (CUPRAC) and Ferric Reducing Antioxidant Power (FRAP)] [38, 40–42], phosphomolybdenum [43], and radical scavenging on [2,2-Diphenyl-1-picrylhydrazyl (DPPH), and 2,2′-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS)] assays [38, 44, 45].

Enzyme inhibition activity

Inhibitory effects of *G. hirsitum* stalk extracts on tyrosinase, cholinesterases (AChE and BChE), α-amylase, and α-glucosidase were analyzed according to the method described previously [38].

Statistical analysis

Statistical evaluation was performed using the SPSS v22.0 software. One-way ANOVA with Tukey's ($\alpha = 0.01$) and Pearson correlation assays were used to analyze the data obtained.

Results and discussion

Phenolic composition

The EtOAc, MeOH, and water extracts obtained from the stalks of *G. hirsutum* were analyzed using spectrophotometric and chromatographic methods.

Results of the spectrophotometric analyses are given in Table 1. It can be seen from the table that the extracts were

Table 1 Amounts of total phenolics and flavonoids in *G. hirsutum* stalk extracts (mean ± SD)

Assays	Ethyl acetate	Methanol	Water
Total phenolics (μmol GAEs/g dry plant)	2.14 ± 0.02[c]	14.38 ± 0.17[a]	13.22 ± 0.25[b]
Total flavonoids (μmol REs/g dry plant)	0.22 ± 0.01[b]	0.61 ± 0.01[a]	0.04 ± 0.01[c]

Data marked with different letters within the same row indicate significant difference statistically ($p < 0.01$)

GAEs gallic acid equivalents, *REs* rutin equivalents

found to contain more phenolic compounds as the polarity increased. The MeOH extract was found to have the highest amount of phenolic compounds (14.38 μmol GAEs/g dp). It has been determined that the water extract contained phenolics as much as the MeOH extract. The amount of phenolics in this extract was found to be 13.22 μmol GAEs/g dp. In this assay, the amount of phenolics was found to be 2.14 μmol GAEs/g dp in the EtOAc extract.

The amounts of total flavonoids in the extracts are also given in Table 1. In this assay, the MeOH extract was found again to have the highest amount of flavonoids (0.61 μmol REs/g dp). It is interesting to point out that the flavonoid content of the EtOAc extract (0.22 μmol REs/g dp) was found to be higher than that of the water extract (0.04 μmol REs/g dp). A two-way ANOVA test revealed that there are significant differences between the total phenolic and flavonoid contents of the extracts ($p < 0.01$).

The extracts were also screened chromatographically to determine the presence or absence of the standard compounds, as given in Table 2. According to the results of chromatographic analyses, none of the extracts were found to contain kaempferol, caffeic acid, rosmarinic acid, chlorogenic acid, luteolin, sinapinic acid, *trans*-cinnamic acid, (+)-catechin, hesperidin, *o*-coumaric acid, and rutin. In general, the results of the chromatographic analysis were found to be consistent with the results obtained from the total phenolic and flavonoid assays. HPLC analyses were resulted in the superiority of the MeOH extract. Except benzoic acid, amounts of the compounds screened were found to be higher in the MeOH extract than those of the water and EtOAc extracts. Protocatechuic acid was found as the most abundant compound in the extracts. The amount of this compound was found to be 31.68, 57.08, and 15.28 µg/g dp in the EtOAc, MeOH, and water extracts, respectively. The MeOH extract was also found to contain considerable amount of apigenin (35.15 µg/g dp), (−)-epicatechin (32.89 µg/g dp), quercetin (27.22 µg/g dp), *p*-hydroxybenzoic acid (22.30 µg/g dp), and gallic acid (21.55 µg/g dp). The EtOAc extract was found to be richer in the majority of the compounds screened than

Table 2 Amounts of selected phytochemicals in *G. hirsutum* stalk extracts (mean ± SD)

No	Phenolic components	Concentration (µg/g dry plant)		
		Ethyl acetate	Methanol	Water
1	Gallic acid	5.04 ± 0.29[b]	21.55 ± 1.51[a]	nd[y]
2	Protocatechuic acid	31.68 ± 1.10[b]	57.08 ± 1.51[a]	15.28 ± 2.26[c]
3	(+)-Catechin	nd	nd	nd
4	*p*-Hydroxybenzoic acid	8.18 ± 0.15[c]	22.30 ± 0.76[a]	19.24 ± 0.17[b]
5	Chlorogenic acid	nd	nd	nd
6	Caffeic acid	nd	nd	nd
7	(−)-Epicatechin	nd	32.89 ± 3.02	nd
8	Syringic acid	3.58 ± 0.15[b]	9.83 ± 0.04[a]	1.70 ± 0.06[c]
9	Vanillin	0.51 ± 0.01[b]	7.18 ± 0.08[a]	nd
10	*p*-Coumaric acid	1.24 ± 0.06[b]	3.78 ± 0.34[a]	nd
11	Ferulic acid	3.43 ± 0.01[a]	3.02 ± 0.02[b]	nd
12	Sinapinic acid	nd	nd	nd
13	Benzoic acid	0.95 ± 0.02[c]	7.56 ± 0.11[b]	11.32 ± 0.17[a]
14	*o*-Coumaric acid	nd	nd	nd
15	Rutin	nd	nd	nd
16	Hesperidin	nd	nd	nd
17	Rosmarinic acid	nd	nd	nd
18	Eriodictyol	0.22 ± 0.01[b]	1.13 ± 0.01[a]	nd
19	*Trans*-cinnamic acid	nd	nd	nd
20	Quercetin	nd	27.22 ± 0.76	nd
21	Luteolin	nd	nd	nd
22	Kaempferol	nd	nd	nd
23	Apigenin	6.28 ± 0.07[b]	35.15 ± 0.38[a]	nd

Data marked with different letters within the same row indicate significant difference ($p < 0.01$)

nd not detected

that of the water extract. Amounts of the compounds in the extracts were found to be different from each other from the statistical point of view ($p < 0.01$).

To the best of our knowledge, some of the compounds belonging to the chemical groups of terpenes (in the flowers, leaves, seeds, and bolls) [16, 19, 20, 25, 46, 47], phenolics (in the flowers, leaves and seeds) [15, 48, 49], fatty acids, carbohydrates, and proteins (in the fibers and seeds) [15, 20, 26–28, 31] have previously been reported. However, no report is available in the literature concerning the phytochemicals of the stalks of this plant. Therefore, data presented here could be assumed as the first report on this issue.

Antioxidant activity

Antioxidant activities of the EtOAc, MeOH, and water extracts obtained from *G. hirsutum* stalks were analyzed using several test systems as follows: metal chelating,

phosphomolybdenum, radical scavenging (on DPPH and ABTS), and reducing power (CUPRAC and FRAP).

The metal chelating activity data of the extracts are given in Table 3. According to the table, the water extract showed the best chelating activity (3.77 µmol EDTAEs/g dp), while the EtOAc extract exhibited the lowest activity potential (0.31 µmol EDTAEs/g dp). The results for this assay were found to be significant at $p = 0.01$ level.

Results of the phosphomolybdenum assay are also given in Table 3. In this assay, the extracts were found to exhibit a different activity pattern than that of the results obtained in the chelating effect assay. The MeOH extract was found to show the highest antioxidant activity (85.61 µmol TEs/g dp). The activity of the water extract was found to be 81.04 µmol TEs/g dp. As seen in the chelating activity assay, the EtOAc extract depicted again the weakest activity (12.82 µmol TEs/g dp). Antioxidant activities of the extracts obtained by this assay were found to be different from each other statistically ($p < 0.01$).

The results obtained from the scavenging activities of the extracts on DPPH and ABTS radicals are set out in Table 4. The extracts were found to exhibit higher radical scavenging activity on ABTS than the activity on DPPH. The water extract showed the highest scavenging activity on both radicals (12.57 and 32.08 µmol TEs/g dp, respectively). Radical scavenging activity of the MeOH extract on DPPH and ABTS radicals was found to be 10.46 and 27.08 µmol TEs/g dp, respectively. As expected, the EtOAc extract showed the weakest radical scavenging activity. There were significant differences between the radical scavenging activities of the extracts ($p < 0.01$).

Table 3 Metal chelating and total antioxidant (by phosphomolybdenum method) activities of *G. hirsutum* stalk extracts (mean ± SD)

Assays	Ethyl acetate	Methanol	Water
Chelating effect (µmol EDTAEs/g dry plant)	0.31 ± 0.01^{c}	1.75 ± 0.02^{b}	3.77 ± 0.01^{a}
Phosphomolybdenum (µmol TEs/g dry plant)	12.82 ± 0.32^{c}	85.61 ± 0.53^{a}	81.04 ± 0.96^{b}

Data marked with different letters within the same row indicate significant difference statistically ($p < 0.01$)

TEs trolox equivalents, *EDTAEs* ethylenediaminetetraacetic acid (disodium salt) equivalents

Table 4 also shows the reducing power potentials of the extracts. The reducing power potentials of the extracts were analyzed using CUPRAC and FRAP methods. Although the results obtained from the both assays were found to be close to each other, the results obtained from FRAP analysis were found to be slightly higher. As observed in the previous test systems, the water extract showed the highest activity (16.44 and 16.57 µmol TEs/g dp, respectively). Reducing power of the EtOAc extract was found to be weak. There were significant differences between the reducing potentials of the extracts ($p < 0.01$).

As far as our literature survey could ascertain, antioxidant activity of *G. hirsutum* stalks has not previously been reported. However, it is possible to find reports concerning the antioxidant activity of the different parts of this plant as well as other *Gossypium* species. Santos et al. [50] have reported the DPPH free radical scavenging, ferric reducing antioxidant power and β-carotene bleaching activities of *G. hirsutum* leaves. Among the extracts, the EtOAc extract showed stronger activity than that of rutin, which was used as the positive control agent. According to this report, the activity of the extract could be attributed to the presence of flavonoids.

Other *Gossypium* species have also been studied for their antioxidant activities. According to the report of Zhao et al. [51], the flower extract of *G. herbaceum* exhibited remarkable scavenging activity on DPPH and ABTS radicals. According to another report carried out using the leaf extract of *G. arboreum*, the water extract significantly protected fibroblast cells against the oxidative damage at doses up to 50 µg/ml [52].

In this study, to set up a statistical relationship between the phytochemicals and activity data obtained from the tests, correlation coefficients between the parameters were also calculated. According to the results of Pearson Correlation Coefficient test, antioxidant activities of the extracts were found to be in correlation with their total phenolic contents. Moreover, *p*-hydroxybenzoic acid and benzoic acid were found to make a significant contribution to the antioxidant activity of the extracts. Therefore, as stated by

Table 4 Radical scavenging and reducing power activities of *G. hirsutum* stalk extracts (mean ± SD)

Assays	Ethyl acetate	Methanol	Water
DPPH (µmol TEs/g dry plant)	1.71 ± 0.01^{c}	10.46 ± 0.02^{b}	12.57 ± 0.02^{a}
ABTS (µmol TEs/g dry plant)	3.99 ± 0.01^{c}	27.08 ± 0.13^{b}	32.08 ± 0.37^{a}
CUPRAC (µmol TEs/g dry plant)	2.02 ± 0.06^{c}	11.35 ± 0.63^{b}	16.44 ± 0.76^{a}
FRAP (µmol TEs/g dry plant)	2.11 ± 0.03^{c}	14.84 ± 0.17^{b}	16.57 ± 0.16^{a}

Data marked with different letters within the same row indicate significant difference statistically ($p < 0.01$)

TEs trolox equivalents

Table 5 Enzyme inhibitory activity of *G. hirsutum* stalk extracts (mean ± SD)

Assays	Ethyl acetate	Methanol	Water
AChE (μmol GALAEs/g dry plant)	na	na	na
BChE (μmol GALAEs/g dry plant)	na	na	na
Tyrosinase (μmol KAEs/g dry plant)	na	na	na
α-Amylase (μmol ACEs/g dry plant)	4.64 ± 0.20[c]	24.65 ± 0.08[a]	13.25 ± 0.18[b]
α-Glucosidase (μmol ACEs/g dry plant)	71.56 ± 5.79[b]	566.09 ± 3.56[a]	682.90 ± 73.75[a]

Data marked with different letters within the same row indicate significant difference statistically ($p < 0.01$)

GALAEs galanthamine equivalents, *KAEs* kojic acid equivalents, *ACEs* acarbose equivalents, *na* not active

Table 6 Correlation coefficients between the assays

	TAP	DPPH	ABTS	CUPRAC	FRAP	MCA	AAIA	AGIA
TFC	0.252[a]	0.015	0.031	−0.156	0.089	−0.409	0.720	0.018
TPC	0.999*	0.964	0.968	0.904	0.981	0.761	0.869	0.965
Protocatechuic acid	0.179	−0.061	−0.044	−0.230	0.014	−0.477	0.665	−0.057
p-Hydroxybenzoic acid	0.989	0.924	0.931	0.846	0.950	0.676	0.922	0.926
Syringic acid	0.349	0.116	0.133	−0.054	0.190	−0.314	0.787	0.120
Benzoic acid	0.912	0.984	0.980	0.999**	0.967	0.968	0.565	0.983

TAP total antioxidant activity by phosphomolybdenum method, *DPPH* DPPH radical scavenging activity, *ABTS* ABTS radical scavenging activity, *CUPRAC* CUPRAC reducing power potential, *FRAP* FRAP reducing power potential, *MCA* metal chelating activity, *AAIA* α-amylase inhibition activity, *AGIA* α-glucosidase inhibition activity, *TPC* total phenolic content, *TFC* total flavonoid content

*$p < 0.05$; **$p < 0.01$

[a]Data represents Pearson correlation coefficient R

the other researchers previously, the antioxidant potential of the extracts could be attributed to the presence of these compounds [53].

Enzyme inhibitory activity

Table 5 shows the inhibitory activities of the extracts on AChE, BChE, tyrosinase, α-amylase, and α-glucosidase. As can be seen from the table, the extracts showed no inhibitory activity on cholinesterases and tyrosinase. When compared, the inhibitory activity of the extracts on α-glucosidase was found to be higher than that of the activity on α-amylase. Inhibitory activities of the water and MeOH extracts were found to be quite strong on α-glucosidase (682.90 and 566.09 μmol ACEs/g dp). The EtOAc extract exhibited the weakest activity in this assay (71.56 μmol ACEs/g dp). In contrast to the results obtained from α-glucosidase inhibitor assay, the MeOH extract showed the highest α-amylase inhibitory activity (24.65 μmol ACEs/g dp). It is followed by the water and EtOAc extracts (13.25 and 4.64 μmol ACEs/g dp, respectively). There were significant differences between the enzyme inhibitory activities of the extracts ($p < 0.01$).

To the best of our knowledge, this is the first study on the inhibitory activity of the stalk extracts of *G. hirsutum*. However, tyrosinase inhibitory activity of the oil of *G. hirsutum* was reported by Nagatsu et al. [54]. According to this report, catechin and quercetin isolated from the oil showed moderate activity. In addition, N-(*p*-coumaryl) serotonin and its 5-*O*-glucoside derivative exhibited weak tyrosinase inhibitory activity.

In addition to data given above, two other *Gossypium* species, *G. herbaceum* and *G. arboretum*, were also studied for their anti-diabetic effects. According to Kazeem et al. [55], water and acetone extracts obtained from the leaves of *G. arboreum* exhibited α-amylase and α-glucosidase inhibitory activity with IC_{50} values of 10.10 mg/ml and 2.75 mg/ml, respectively. Kazeem et al. [55] found the extracts to be rich in tannins and steroids and they claimed that these compounds might be responsible for the activity observed.

On the other hand, Rifat-uz-Zaman and Ghaffar [56] have found that the water and ethanol extracts obtained from the seeds of *G. herbaceum* have promising anti-diabetic and hypolipidemic effects and could be effective tool against the development, progression, and complication of diabetes mellitus.

Enzyme inhibitory activity of *G. herbaceum* has also been studied by Zhao et al. [51]. According to the results of this study, the extract obtained from the flowers is an efficient AChE inhibitory agent, and thus, it may be helpful in preventing or alleviating the patients suffering from Alzheimer's disease.

According to the correlational coefficients given in Table 6, there appears to be a linear relationship between the total phenolic contents of the extracts and the α-amylase/α-glucosidase inhibitory activities. In addition, as seen in the antioxidant activity section of this study, *p*-hydroxybenzoic and benzoic acids seem to contribute the inhibitory activity of the extracts.

Conclusions

As can be seen from the data presented, the MeOH and water extracts of *G. hirsutum* exhibited promising antioxidant and α-amylase/α-glucosidase inhibitory activity. This means that the stalk, which is the post-harvest field trash of the cotton cultivation, is an alternative source of bioactive molecules and can be used in pharmaceutical and food industries for its anti-diabetic and antioxidant activity as well as its use in particleboard, wood adhesive, ethanol, and briquette production. Thus, it will be possible to transform the stalks, one of the key by-products of the cotton industry, into the high-value industrial products having economic importance.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human and animal rights This article does not contain any studies with human or animal subjects.

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