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Original Article

Spectroscopic Screening of Dexamethasone and Cyproheptadine Adulteration in Weight Gaining Products Marketed in Aden, Yemen

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Abstract

Background: Weight-gaining (WG) products are either medicine or herbal products that have been used intensively by the young and adolescents in Yemen. These products may contain undeclared potentially toxic ingredients that can lead to several health problems and diseases on long-term usage. This study was intended to evaluate the presence of some undeclared pharmaceuticals, dexamethasone (DX) and cyproheptadine (CPR), in WG products in Aden, Yemen.

Methods: The detection of DX & CPR in WG products was evaluated using UV& Fourier transform infrared (FT-IR) spectroscopy. Also, phytochemical analysis was carried out for herbal products.

Findings: The study indicated the presence of CPR in Tab-II, honey mixture, and capsules in the range between 0.10%-102.6%. A lower percentage was detected in the honey mixture and a higher percentage in Tab-2. DX was only detected in Tab-I (102.87%).

Conclusion: It can be concluded that WG products may contain undeclared amounts of DX and CPR. Stricter regulations must be implemented for the usage and distribution of these products to avoid potential long-term adverse consequences.

Keywords: Adulteration, Cyproheptadine, Dexamethasone, Weight-gain

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Introduction

People in developed countries suffer from obesity; however, Yemenis and others in some developing countries are mostly underweight. Therefore, weight-gaining products (WG), either pharmaceutical, natural, or local mixture, are widely used by the young and adolescents. Herbal medicines and products are used for well-being and health in several conditions such as addiction therapy, enhancement of sexual capabilities, bodybuilding, improvement of athletic performance, etc.[1,2] There is an increasing trend in addiction to herbal products for acquiring the desired body shape across all ages, especially the young and adolescents.[3]

In Yemen, herbs are sold by street sellers or in "Attarah" stores, without any official control or supervision. As a result, it is possible to obtain poor quality, impure, or contaminated herbs with adverse health effects and/or lethal toxicity. According to a survey, between 65% and 80 % of people in poor nations utilize herbs to cure illnesses due to poverty and the lack of access to allopathic medications.[4] The general public can buy pharmaceuticals and herbal items over the counter without a prescription and online on a variety of websites, virtual marketplaces, and social media.

As a result of the absence of censorship by the governorate, traditional medicine factories may fraudulently increase their sales by adding chemical drugs to their products to achieve the intended effects,[5] highlighting the importance of monitoring and controlling local hand-made products and supplements for efficiency and safety.[6-8] Substandard, spurious, falsely labeled, falsified, and counterfeit (SSFFC) pharmaceuticals have been officially recognized by the World Health Organization (WHO) as products with incorrect active pharmaceutical ingredients (APIs).[9]

Some of these products contain added pharmaceuticals such as dexamethasone (DX), cyproheptadine (CPR), and others. DX is an extremely selective glucocorticoid with weight gain product as one of its side effects, encouraging manufacturers and herbal producers to add DX to their herbal preparations to meet customers' demands for quick and cheat weight gain. However, its other effects include an increase in blood pressure and blood sugar levels, a decrease in immune responses, and elevated risk of bone loss, therefore, it should be administered under medical supervision. According to the FDA, one of the Chinese medicines containing DX can have negative effects like

moonfaced.[10]

Cyproheptadine is a histamine H1 blocker acting as a serotonin antagonist and an anticholinergic agent used for the treatment of several types of allergies. This compound was noted to cause unexpected WG.[11] In Kinshasa, the use of CPR for WG has been approved among the general population and to acquire a "round physical shape". In fact, its side effects include increased desire for food and weight gain. Consequently, CPR is used to treat anorexia, cachexia, and severe malnutrition. The effect of CPR on WG has been approved in some studies.[12-14] In Yemen, people who want to gain weight can buy this medicine in the market as labeled appetite stimulant and supplied abusively without a doctor's prescription.

In Yemen, only one master's thesis examined the adulteration and contamination of WG capsules. The study indicated the presence of CPR, DX, prednisolone, and betamethasone in these capsules. The dose of some of these medicines even exceeded the recommended level.[15]

The adulteration of herbal products with medicines has been subjected to extensive studies. For instance, a study was carried out to detect the presence of CPR in 15 herbal appetizing tonic supplements using an HPLC-UV detector, and the concentration of CPR was reported between 1.68 and 40.56 mg/g.[16] A study in Iran also identified the adulteration of 60 herbal drug samples with CPR, DX, sildenafil, tramadol, caffeine, and acetaminophen using UHPLC and GC/MS methods, reporting the concentration of CPY and DX as 0.2–67 and 5.5–10.1 mg/tablet or capsule, respectively.[17] Another study in Iran detected corticosteroids, phosphodiesterase inhibitors (PDH-5), sildenafil, and tadalafil as counterfeit in 10 WG herbal products. The amount of DX was between 37.58 and 145.42 µg /mL per pill or capsule.[18] In Indonesia, a study revealed the presence of DX in two herbal samples using the HPLC-densitometry method. The average amounts of DX in two samples were 0.23% and 0.25%, respectively. A study revealed the presence of anabolic steroids and clenbuterol at trace levels in 30 dietary supplements measured by liquid chromatography-mass spectrometry (LC-MS).[19] Another study used HPLC-MS/MS to analyze various food and supplement samples marketed for the treatment of arthritis, bone aches, and joint pain from local and online Korean stores. Six compounds were detected as impurities in some products, including DX (45.1%), cortisone-21-acetate and prednisone-21-acetate (16.2%), and betamethasone (14.4%).[20]

The study of these products' ingredients is necessary in Yemen. The current study was carried out to provide information about the presence or absence of pharmaceutical active ingredients such as; DX and CPR using UV spectrometry and Fourier transform infrared (FT-IR) in locally mixed WG products, imported herbal pills, and tablets sold online or by local traders. We also assessed the phytochemical properties of these herbal products.

Material and Methods

Reagents

Five different WG products were collected from local pharmacies, honey, online, and Al-attar shops in Aden City, Yemen. The information related to these products is listed in Table 1. The selection was based on the extent of distribution and frequency of usage. All reagents and solvents used were of analytical grade.

Instruments

The information related to the instruments used in this study is listed in Table 2.

Solvent selection

The solubility of DX & CPR was determined in methanol, and the absorbance spectrum of DX & CPR was determined in the range of 200- 400 nm.

Determination of DX Peak absorption

For this purpose, 0.5 mg of DX sodium phosphate was transferred to a 50 mL volumetric flask, and 20 mL of methanol was added to the flask. The flask was sonicated for 10 minutes to solubilize the drug, and the volume reached 50 mL using methanol (100 ppm). After filtration, 1 mL of the filtrate was transferred to a 10 mL volumetric flask and diluted to mark with methanol to obtain a 10-ppm concentrated solution. Then the solution was scanned in the range of 200-400 nm to determine the wavelength of maximum absorption.[21]

Calibration curve of DX

Aliquots of the standard solution of DX were transferred into a series of 10 mL volumetric flasks. The required amount of methanol was added to each flask, and finally, the volume in each flask was brought up to 10 mL with methanol to prepare concentrations ranging from 8 to 28 µg/mL. Then absorbance was measured at 243 nm against the reagent blank.

Determination of CPR peak absorption

An accurately weighed quantity of 10 mg CPR HCl was transferred into a 100 mL volumetric flask, dissolved in 50 mL of methanol, and sonicated for 10 minutes. The volume was reached up to the mark with methanol to obtain a solution with the 100-ppm concentration. An appropriately diluted solution was prepared from the standard stock solution containing 10 ppm of CPR HCL. Final scanning was in the range of 200-400 nm.[22]

Calibration curve of CPR

Aliquots of the standard solution of CPR ranging from 10-35 ppm were transferred into a series of 10 mL volumetric flasks. To each flask, the required amount of methanol

Table 1. Information of two tablets of DX and CPR and five WG products

Brand code	Made in	Content	Manufacture date & expiration date	Batch No
Powder herbs	Yemen-Aden	No label	Mfg: Jun-2021 Exp: Jun-2024	-
Honey mixture	Yemen	Honey, Roya Jelly, Pollen, Ginseng, Nuts, Herbs for fatting	Mfg: 26-5 2022 Exp: 26-5-2023	-
Capsules®	China	Angelica, chuanxiong, Cordyceps, Polygonum multiform, gecko, cinnamon, *Morinda Officinalis*, pilose antler, *Eucommia ulmoides*, ginseng, *Gastrodia elata*, *Atractylodes macrocephala*, Beiqi yam, *Rehmannia glutinosa*, medlar, Anemarrhena, Yunling, acid proof jujube kernel and licorice	-	-
Tab-I	Egypt	Unknown	-	-
Tab-II	Egypt	Unknown	-	-

Table 2. List of instruments used in the study

Instrument	The Manufacture, Company
Electronic balance	A&D Company LTD, Japan, HR-250
Oven	VACIOTEM-T SELECTA, Spin
Electronic shaker	Patterson Scientific LTD, Germany, KS130
Water bath	Clifton, England, NE2-56D
UV-Visible spectroscopy	(Lasany® advanced microprocessor UV-VIS-L1-295
Centrifuge	P-Selecta, Mixtasel
Vortex	Heidolph Reax Top, Germany
pH meter	Inolab WTW, Germany
FT-IR spectroscopy	PerkinElmer ULTRA TWO, USA
UV-lamb	Model UVL-21 Long eave 365 nm, Upland, CA 91786 UAS

was added, and finally, the volume in each flask was brought up to 10 mL with methanol. Then absorbance was measured at 285 nm against the reagent blank.

Sample analysis; tablets

One tablet was weighed accurately, finely powdered, and transferred to a 20 mL volumetric flask, and then 20 mL of methanol was added. The flask was sonicated for 10 min to solubilize the drug, and then the volume reached 50 mL with methanol. After filtration, 4 mL of the filtrate was transferred into a 10 mL volumetric flask, and it was diluted with methanol. The absorbance of this solution was measured at 243 nm & 285 nm against the corresponding blank.

Sample analysis; capsules

One capsule (0.4 gm powder) was weighed and transferred to a 20 mL volumetric flask, and then 20 mL of methanol was added. The flask was shaken overnight for extraction. After filtration, 0.5 mL of the filtrate was transferred into a 10 mL volumetric flask, and then it was diluted with methanol. The absorbance of the solution was measured at 243 & 285 nm against the corresponding blank.

Analysis of herbal powder

The herbal powder (0.5 g) was weighed accurately and transferred into a 20 mL volumetric flask, and 20 mL of methanol was added. The flask was shaken overnight for extraction. After filtration, 0.25 mL of the filtrate was transferred to a 10 mL volumetric flask and diluted with methanol. The absorbance of this solution was recorded at 243 & 285 nm against the corresponding blank.

Analysis of honey

Honey (0.5 g) was weighed accurately and transferred into a 20 mL volumetric flask; 20 mL of methanol was added. The flask was shaken overnight for extraction. After filtration, the absorbance of this solution was measured at 243 & 285 nm against the corresponding blank.

Fourier transform infrared spectroscopy

Solid grounded samples of tablets, methanol extractions of capsules, honey, and herbal powder were prepared and scanned in the range of 400 -4000 cm^{-1} at ambient temperature.

Phytochemical analysis

Phytochemical tests for carbohydrates, alkaloids, amino acids, flavonoids, etc. were carried out according to standard procedures.[23-24]

Extract *preparation*

Herbal powder (20 g) and capsule ingredients (10 g) were dissolved in 200 mL and 100 mL methanol, respectively, stirred overnight, and the solvent was finally evaporated.

Results

UV-spectroscopy for detecting DX and CPR

DX and CPR were dissolved in methanol and examined alone to determine their maximum absorbance. The λ_{max} of the drugs was found to be 243 nm and 285 nm for DX and CPR, respectively.

Method validation

Method validation was performed as per ICH guidelines Q2 (R1).[25] The linearity of this method was checked for DX at the concentrations of 8, 12, 16, 20, 24, and 28 ppm and for CPR at 10,15, 20, 25, 30, and 35 ppm. The

investigated concentrations followed Beer's Lambert law. Three sets were evaluated for linearity.

The LOD and LOQ were calculated as k = 3.3 and k = 10, respectively. All validation parameters are illustrated in Table 3.

Precision (intra-day and inter-day) assessment results are demonstrated in Table 4; high reproducibility with % Relative Standard Deviation (RSD) below 2.0 was observed, verifying the precision of the method.

Accuracy is the estimation of the degree of closeness of the determined value to the real value. The result of accuracy is represented in Table 5.

Organoleptic properties

The evaluation of tablets and capsules in this study revealed that the samples had a uniform color with no distinct or pungent odor. The powder had an herbal odor with the scent of fenugreek while honey had a bitter taste and a homogenous appearance.

pH values

The pH of the honey mixture was 4.65 ± 0.122.

Detection of DX &CPR in WG products

The products were analyzed to quantify DX and CPR by UV spectrophotometry (Table 3). The presence of DX and CPR was verified by comparing the maximum absorbance of samples with those of DX and CPR standards. This study indicated the presence of CPR in Tab-II, capsule, and honey in average amounts of 102.6% (4.10 mg) ± 1.71, 2.63% (0.021 mg) ± 0.04, and 0.1 (0.025 mg) ± 0.001, respectively. A lower % of the drug was found in honey, and a higher % was observed in Tab-I. The DX was only detected in Tab-I with an average amount of 102.87% (0.51 mg) ±1.18. The results are represented in Table 6. The UV spectra of five products are illustrated in Figures 1 to 5.

The Tab-I and Tab-II were confirmed to be pure DX and CPR tablets because their UV and IR spectra matched with those of DX and CPR tablets, respectively. The IR-Spectra of WG Products & DX, CPR tablet have been interpreted in Table 7. The respective IR spectra are shown in Figures 6 and 7 (a-c).

The average weights and thickness of DX and CPR tablets were evaluated. The average weights of DX and CPR were 0.10422 and 0.2189 gm, respectively, which were similar to the average weights of Tab-I and Tab-II (0.10678 and 0.2272 gm, respectively). The thickness values of DX and CPR were 2.192 and 2.718 mm, respectively, compared to the respective values of 2.23 and 2.846 mm for Tab-I and Tab-II. Also, the organoleptic evaluation revealed the similarity of both products. The social media seller claimed that Tab-I & II were exported from Egypt to promote their goods, but they seemingly deceived their customers and sold them DX and CPR tablets as WG products. Thirty tablets with 10 000 YR (US$ 8.3), and using them without a physician's supervision could have many side effects.

Phytochemical evaluation of WG herbal products

The content of powders & capsules was extracted by methanol (99.8 %), with yields of 9.78% for 20 gm powder and 2.1% for 10 gm capsule. The color of the extract was yellowish-brown and green for powder and capsules, respectively.

Qualitative phytochemical analysis

Phytochemical screening of the methanolic extracts of powder & capsules was carried out (Table 8). The capsules were rich in carbohydrates, resins, amino acids, lignin, tannins, triterpenoid, phytosterol, alkaloids, and coumarin, while cholesterol, fixed oils and fats, and flavonoids were not present in capsules. In the case of powder, carbohydrates, resin, amino acids, cholesterol, fixed oils, and fats, tannins, flavonoids, triterpenoids, phytosterol, and alkaloids were detected, while lignin and coumarin were not among the ingredients. So, the samples contained herbal ingredients in addition to CPR, as evidenced by UV spectroscopy.

Thin layer chromatography

Thin layer chromatography (silica gel G 60 F254 TLC plates of layer thickness 0.2 mm, Allugram, Germany) was carried out for the prepared extracts to determine *Rf* values. The solvent system that gave the maximum number of spots for the extract was adopted.

Table 3. Validation parameters for the developed method

DX		CPR	
Validation parameters	**Data (Mean ± SD)**	**Validation parameters**	**Data (Mean ± SD)**
ƛ max (nm)	243 nm	ƛ max (nm)	285 nm
Range (ppm)	8.0-28 ppm	Range (ppm)	10-35 ppm
Correlation coefficient	0.9997 ± 3.24208E-05	Correlation coefficient	0.9995 ±0.00024
Intercept	-0.0747 ± 0.00481	Intercept	0.1845 ± 0.0061
Slope	0.0364 ± 0.0002	Slope	0.0339 ± 0.0003
LOD (ppm)	0.626 ± 0.0400 ppm	LOD (ppm)	1.074 ± 0.2571ppm
LOQ (ppm)	1.899 ± 0.1214	LOQ (ppm)	3.255 ± 0.7793ppm

Table 4. Statistical evaluation of precision parameters for DX and CPR

Parameters	Lower Conc. (8 ppm) (n=9)	Medium Conc. (16 ppm) (n=9)	High Conc. (24 ppm) (n=9)
DX			
Average	0.2155	0.5124	0.8044
SD	0.0013	0.0088	0.0093
RSD%	0.62	1.72	1.15
Parameters	**Lower Conc. (10 ppm) (n=9)**	**Medium Conc. (20 ppm) (n=9)**	**High Conc. (30 ppm) (n=9)**
CPR			
Average	0.1462	0.4948	0.8330
SD	0.00030	0.0054	0.0025
RSD%	0.21	1.11	0.34

Table 5. Statistical evaluation of accuracy for DX and CPR

Product	Theoretical conc. of the spiked sample (ppm) DX	Conc. of spiked sample ± SD (ppm) (n=3)	Recovery ± SD (%)	%RSD
Tablet	8	8.08 ±0.14	101.05 ±1.7	1.68
	16	16.34 ±0.14	102.14±0.88	0.86
	24	24.76 ±0.03	103.19 ±0.15	0.14
Capsule	8	7.99 ±0.08	99.98±1.03	1.03
	16	16.57±0.10	103.58±0.68	0.66
	24	24.68±0.19	102.83±0.25	0.79
Honey	8	8.08±0.13	101.05±1.70	1.68
	16	16.64±0.02	104.02±0.13	0.12
	24	24.94±0.34	103.95±1.43	1.38
Conc. of a sample (ppm)	**Theoretical conc. of the spiked sample (ppm) CPR**	**Conc. of spiked sample ± SD (ppm) (n=3)**	**Recovery ± SD (%)**	**%RSD**
Tablet	10	9.92 ±0.15	99.21 ±0.15	1.49
	20	19.93 ±0.18	99.69±0.15	0.90
	30	30.46 ±0.62	101.53 ±2.07	2.04
Capsule	10	10.27 ±0.18	102.7±1.84	1.79
	20	20.18±0.28	100.91±1.40	1.39
	30	29.92±0.07	99.74±0.25	0.26
Honey	10	9.87 ±0.14	98.76±1.45	1.47
	20	20.28±0.07	101.44±1.56	1.54
	30	30.49±0.07	101.65±1.57	1.55

The best solvent applicable for the methanolic 99.8% extract was chloroform-methanol (9:1) mixture, where 11 spots in the methanolic 99.8 % extract of capsules and 5 spots in the methanolic 99.8 % extract of powder were observed. Images were taken in daylight and in a UV chamber, and *Rf* values of the developed spots were calculated, as well as their colors (Table 9).

Discussion

Adulteration using synthetic pharmaceuticals can be fatal, especially if such substances can combine with other medications and exacerbate preexisting medical conditions. The lack of or weak governmental quality control of drugs encourages the production of unregistered medications and selling them on the market or via social media. As a result, it is critical to identify any unreported synthetic pharmaceuticals in herbal remedies or other unregistered medications.

A former study was carried out in Aden, Yemen, to detect CPR and some corticosteroids such as DX, betamethasone, and prednisolone, in only two capsules. The current study evaluated five WG products. Most of these products were imported from countries that had

Table 6. The % of DX and CPR in the WG products analyzed

Products	% of DX ± SD	% of CPR ± SD
Tab-I	102.87±1.18	ND
Tab-II	ND	102.6% ± 1.71
Capsule	ND	2.63% ± 0.04
Powder	ND	ND
Honey mixture	ND	0.10 %± 0.0015

ND, not detected.

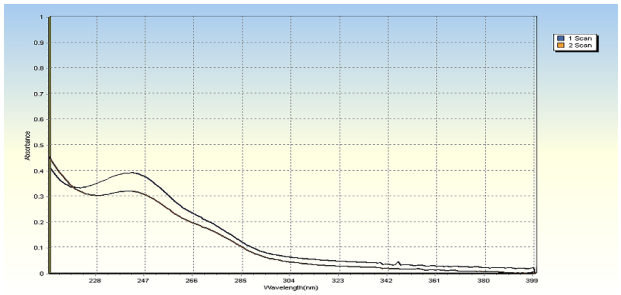

Figure 1. The UV spectrum of Tab-I and DX in methanol

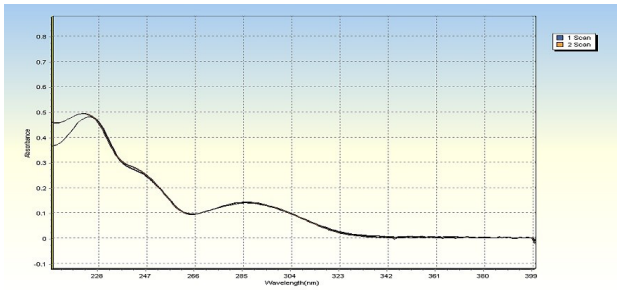

Figure 2. The UV spectrum of Tab-II and CPR in methanol

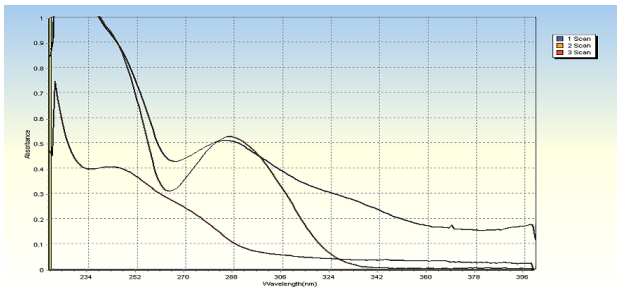

Figure 3. The UV spectrum of the capsule, DX, and CPR in methanol

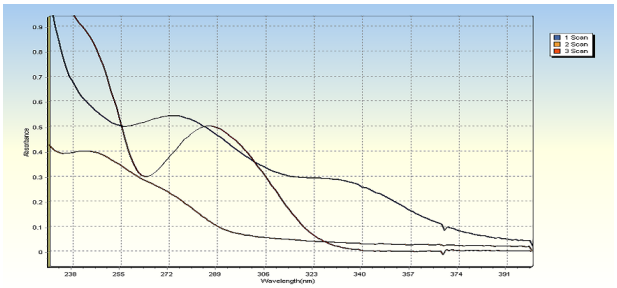

Figure 4. The UV spectrum of powder, DX, and CPR in methanol

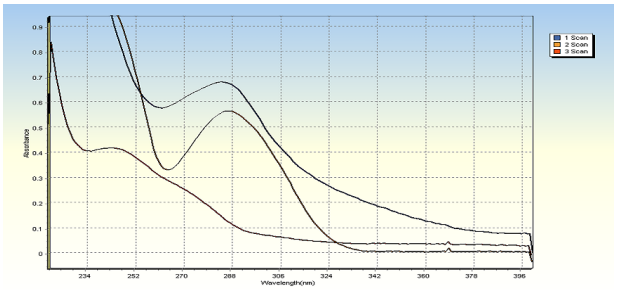

Figure 5. The UV spectrum of honey mixture, DX, and CPR in methanol

weak regulatory inspections and screening, as well as non-standard manufacturing. Some of these products were made locally by mixing several herbs, honey, and nuts with no quality quality assessment. These products may be adulterated by some pharmaceuticals to help obtain WG more quickly and efficiently.

Depending on its botanical source and other parameters (e.g., the pH of the nectar, the soil or plant connection, and the concentration of various acids and minerals like calcium, sodium, potassium, and other ash elements), the pH of honey can vary from 3.5 to 5.5,[26] and any major deviation to this range could be a sign of adulteration or fermentation.[27] In this study, the pH of the honey mixture was within the recommended range.

The comparison of the IR spectra of selected products with those of CPR and DX tablets revealed a clear match between DX and Tab-I spectra (Figure 6a). Also, Tab-II and CPR spectra were identical (Figure 6b). The end part of the CPR spectrum showed overlap due to the presence of excipients with the pharmaceutical dosage form, affecting the spectrum's general shape.[28] In the case of the honey mixture (methanolic extract), the spectrum matched with that of CPR in only three regions, 3224 Cm^{-1} (OH stretching), 1647 Cm^{-1} (C=O stretching), and 1359 Cm^{-1} (CH3 bending). This may be due to the presence of other constituents in the mixture. The methanolic extract of the powder showed a spectrum similar to CPR in two regions: 2854 Cm^{-1} (NH stretching) & 1709 Cm^{-1} (C=O stretching), which might also be due to the presence of other constituents.

The powder extract showed one well-defined peak at 276 nm and a small peak at 332 nm. The capsule spectrum showed a maximum absorbance of 285 nm, which was similar to that of CPR. Also, the honey mixture's spectrum showed maximum absorbance at 285 nm, which matched the spectrum of CPR.

A former study carried out in Aden, Yemen, investigating the capsules present in local markets, indicated that the first capsule contained CPR (1.8 mg), DX (6.17 mg), prednisolone (0.2 mg), and betamethasone (0.91 mg), while the second capsule contained CPR (7.1 mg), DX (0.051 mg), prednisolone (14.4 mg), and betamethasone (1.83 mg). However, there was a difference in the % of CPR between the above-mentioned report and the present study. We reported the presence of CPR in 2.63% (0.021 mg) ± 0.04, while the previous study indicated that CPR was present in 1.8 mg in capsule-1 and 7.1 mg in capsule-2. The difference may be due to the

Table 7. The Interpretation of IR-Spectra of WG Products & DX, CPR Tablet

Name of products	Functional groups	Wavenumber cm^{-1}
DX Tab.	OH stretching	3333
	OH stretching	2900
	Para-disub. Benzene	898
	Primary alcohol	1053
CPR Tab.	carboxylic acid OH stretching	3332
	OH stretching	3224
	NH stretching	2900
	C=O stretching	1647
	CH3 bending	1359
	C- F stretching	1070
	C-Cl stretching	631
Tab-I	OH stretching	3333
	OH stretching	2899
	Para-disub. Benzene	894
	Primary alcohol	1053
Tab-II	NH stretching	3332
	CH stretching	2900
	S=O stretching	1315-1160
	C-N stretching	1029
	halo compound	552
Capsule	OH stretching	3281
	=CH stretch	1011
Powder	NH stretching	2923-2853
	NH stretching	2854
	C=O stretching	1709
	CH_2 bending	1464
	C-O-C stretching	1050
	C-Br stretching	720
Honey mixture	OH stretching	3252
	C=O stretching	1645
	CH_3 bending	1415
	C-N stretching	1028

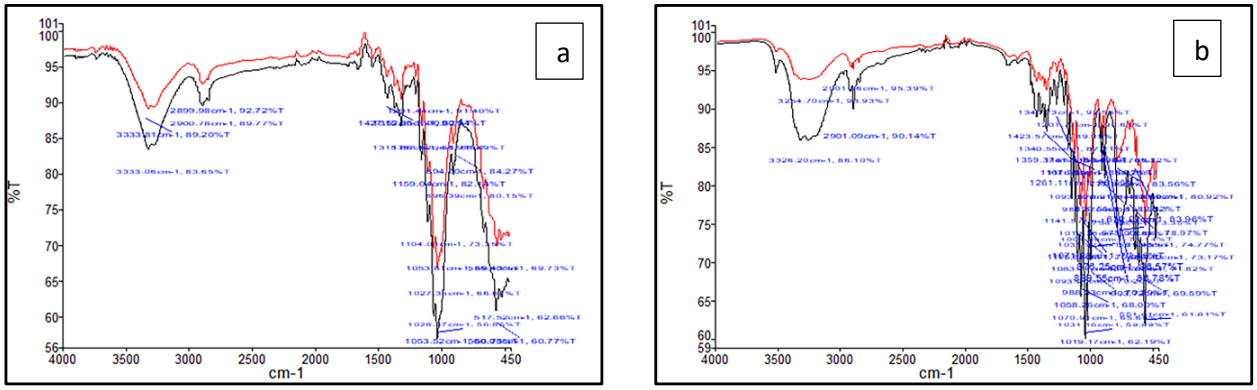

Figure 6. (a) The IR spectrum of Tab-I and DX Tab, (b) The IR spectrum of Tab-II and CPR Tab

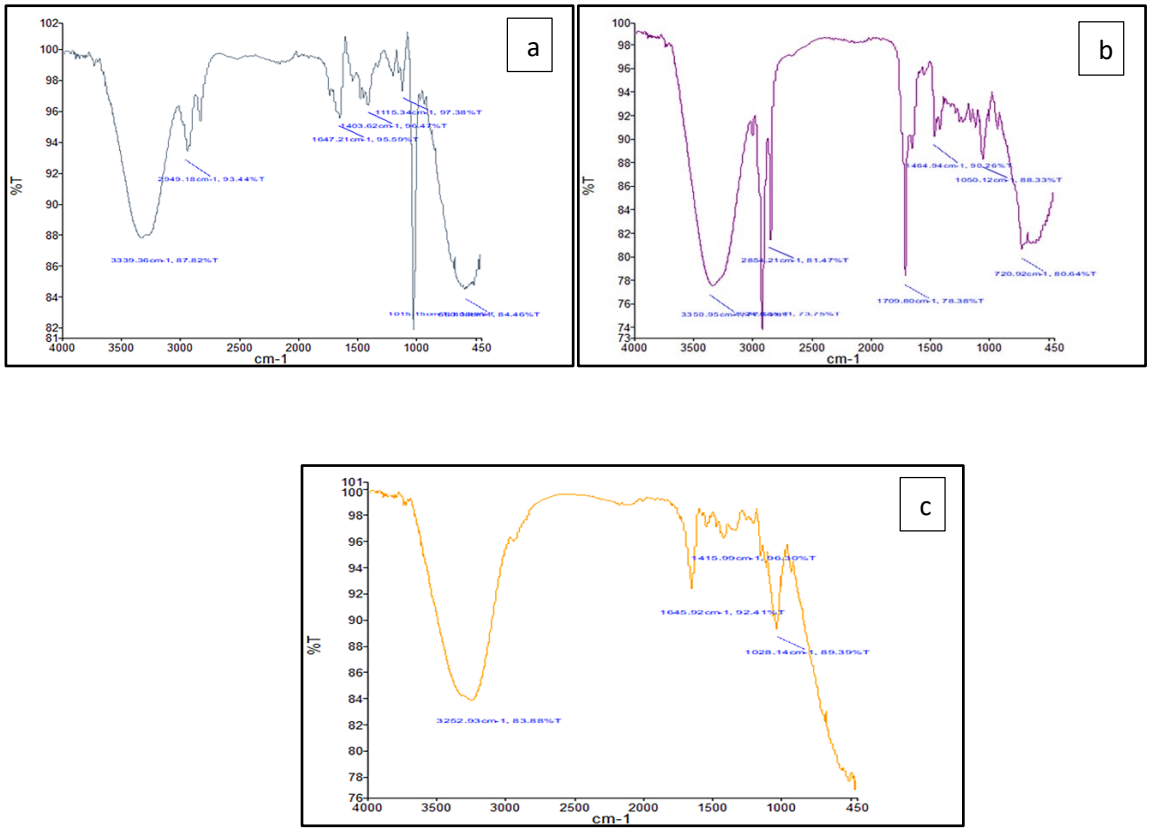

Figure 7. (a) The IR spectrum of capsule extract in methanol, (b) The IR spectrum of powder extract in methanol, (c) The IR spectrum of honey mixture extract in methanol

presence of two types of this product in the market (i.e., original and fake or of low-quality). Because a long time has passed since the previous study, which was carried out in 2016, there might be a change in the trader and content of capsules. Also, the current study did not detect the presence of any corticosteroids in the capsule. This discrepancy may be due to the use of UV-spectroscopy in the current study and HPLC in the previous study.

The percentage of CPR was lower than in the previous study, where CPR was detected in 15 samples purchased from different herbal shops. There was no declaration of the presence of CPR on labels. The amount of CPR ranged between 1.68- and 40.56 mg/g,[16] which was lower than the ratio reported in a study in Iran (0.2–67 and 5.5–10.1 mg/tablet or capsule for CPR and DX, respectively).[17] Another study in Iran detected the presence of DX in ten herbal products. The amount of DX was between 37.58 and 145.42 (µg/mL) per pill or capsule, which was much higher than the value reported in the current study. A study in Iran revealed the presence of unapproved medications in powders, formulations, capsules, and syrups. Most of these supplements consisted of glucocorticoids, testosterone,

Table 8. Phytochemical ingredients of methanolic extracts of capsules & powders

Test	Observation		Result	
	Cap.	Herb	Cap.	Herb
Carbohydrate				
Molisch's test	Violet ring	Violet ring	+ + +	+ + +
Fehling's test	Brick Red ppt	Brick Red ppt	+ +	+ +
Benedict's test	Brick Red ppt	Brick Red ppt	+ +	+ +
Resin: Turbidity	Turbid	Turbid	+ +	+ +
Amino acid: Ninhydrin	Dark bluish turquoise solution	Light violet Purple solution	+ + +	+ + +
Cholesterol	No change	Reddish orange solution	-- -	+ +
Lignin: Labat's test	Olive green color	No change	+	-- -
Fixed oil and at: Spot test	No change	Transplant spot	- - -	+
Tannins				
$FeCl_3$	Dark greenish blue	Dark greenish blue	+ + +	+ + +
Lead acetate	White ppt	White ppt	+ + +	+ + +
Identification of saponins: Foam test	No change	No change	- - -	- - -
Flavonoids				
Shinoda's test	No change	Yellowish color	-- -	+ + +
Lead acetate	No change	Yellow ppt	-- -	+ + +
NaOH	No change	Yellow color	- - -	+ + +
Triterpenoid and phytosterol				
Liberman's	Brown ring + green upper layer	-Brown ring + No green upper layer	+ + +	+ + +
Salkowski's	Reddish brown ring	-Reddish brown ring	+ + +	+ + +
Alkaloid:				
Dragendroff 's	Orang brown ppt	Orang brown ppt	+ + +	+ + +
Wegner's	Reddish brown ppt	Reddish brown ppt	+ + +	+ + +
Mayer's	Creamy shit ppt	Creamy shit ppt	+ + +	+ + +
Coumarin: NaOH paper test	Yellow fluoresce -under UV	No change	+ + +	- - -

+ + + = Most intense, + + = moderately intense, + = Least intense, - = absent.

Table 9. Thin layer chromatography analysis of methanolic 99.8% extract of capsules and herbs

Extract or fraction	No. of spots	Rf values	Color of the spot at daily light	Color of the spot at 254 nm	Color of the spot at 365 nm
Methanolic capsule extract	11	0.89	Light green	Quenching	Carmine red
		0.87			Pinkish white fluorescent
		0.85			Burgundy red
		0.79	Not visible	Non-Quenching	Red
		0.74			Burgundy red
		0.59			
		0.55	Light green		Carmine red
		0.48		Quenching	
		0.32	Not visible		
		0.21		Non-Quenching	Purple
		0.14			
Methanolic extract of powder	5	0.75	Not visible	Quenching	Sky fluorescent
		0.72		Non-Quenching	blue
		0.25			
		0.18		Quenching	
		0.09			

antipsychotics, CPR, hormonal components, and other medications triggering WG.[4]

A study conducted in Korea revealed the presence of DX (45.1%), cortisone-21-acetate, prednisone-21-acetate (16.2%), and betamethasone (14.4%), which had high concentrations in some samples.[20] These values were much higher than those observed in the current study. Another study in Indonesia detected DX in the range of 0.23% and 0.25%, while the present study revealed that CPR content was 102.87% for Tab-I (a product sold on social media) and 102.6% for Tab-II. Therefore, DX & CPR tablets are commonly sold as WG products in Aden, Yemen, mainly because there is no regulation or strict control on these websites.

The most important side effects of DX include an increase in blood sugar levels, bone loss, childhood growth restriction, fat accumulation in certain body parts, and weakening of the immune system, increasing propensity to infections [29]. As noted, almost all samples contained CPR, which may be due to its well-tolerability and safer profile than corticosteroids, so it is commonly popular among those seeking weight gain.[30]

Conclusion

Weight gain products are supplementary nutrients or medicines that are used voluntarily to increase weight and remain healthy. A number of these products contain a diversity of unlabeled active ingredients that are highly toxic. Arab countries are characterized by a culture of weight gain, especially among girls who consider it a type of beauty. Most of the products examined contained CPR in varying amounts except for Tab-I and powders. DX was only detected in Tab-I. The unrestricted use of unregistered herbal WG products containing DX can undoubtedly raise health risks; therefore, authorities need to closely monitor herbal goods that are sold in the community. Also, there should be awareness campaigns for the public about the side effects of DX and CPR upon prolonged use.

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Competing Interests

The authors declared no conflict of interest.

Ethical Approval

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