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# CHROMATOGRAPHIC ANALYSIS OF ORCHID EXTRACTS AND QUANTUM CHEMICAL CALCULATIONS OF INDIVIDUAL COMPONENTS INTERACTION WITH SILICA

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**Abstract.** The aim of the work was to identify the main components of orchid extracts and to study their interaction with silica. Composition of sixteen orchid extracts was investigated by means of high performance liquid chromatography and laser desorption/ionization mass spectrometry; as it was shown in this study, flavonoids and phenolic acids were the main bioactive compounds available in the extracts. The interaction between various phenols and silica silanol groups was studied by quantum chemical method. Results show that the strength of interaction of phenols with silica increased in the following order: ferullic, feruloylquinic and fertaric acids< kaempferol, apingenin<< chlorogenic and caffeic acids, rhamnetin, quercetin, luteolin, epicatechin gallate. The common feature of compounds characterized by the strongest interaction with silanol groups is the presence of a phenol ring with two neighbouring hydroxyl groups. The hydrogen bonds formed between these groups and silanol groups are much shorter (about 0.17 nm) than those formed by other hydroxyl groups of phenols (up to 0.28 nm).

**Keywords:** orchid extract, phenolic compound, fumed silica, quantum chemical calculation.

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## Introduction

The plants are known to be a valuable source of low-toxicity biologically active substances [1-3]. Among these substances, phenolic compounds possessing antioxidant or antimicrobial properties appear to be particularly attractive for practical application [4,5]. The orchid plants are used in traditional medicine of many countries and are known to contain high amounts of phenolic compounds [6-8]. It was reported that the content of phenols in orchids reached up to 12 mg of gallic acid equivalent per 1 g of dry weight, with the composition of the extracts being dependent on the climatic and external conditions of plants growing [9,10]. The majority of orchids were found to contain a significant amount of phenols such as hydroxybenzoic acids, hydroxycinnamic acids and flavonoids in the glycoside form [6].

Nowadays, half of all medical drugs, dietary supplements and herbal medicines are produced from natural sources, with phenols being the main active components of most of these drugs [11,12]. However, direct oral use of phenolic compounds has some disadvantages. Due to low solubility of phenols in water, as well as their poor gastrointestinal stability and absorbency, the compounds were shown to have low bioeffectiveness [13,14]. To improve the efficiency of plant-derived drugs, a number of drug delivery systems were developed [14-17], with fumed silica being one of the possible auxiliary ingredients used as carrier for plant extracts and plant-derived bioactive molecules [18,19]. Immobilization of biologically active substances on the silica surface offers the possibility of introducing hydrophobic compounds in aqueous solutions and hydrophilic substances in lipophilic media [20]. Inclusion of bioactive compounds in silica-based composites improves the compounds storage stability as compared to pure extracts/substances [19].

In some cases, the presence of silica can decelerate the release of the drug into solution, thus providing bioactive substances with elongated effect [18,20]. The properties of composites consisting of bioactive compounds and fumed silica apparently depend on the strength of interaction of compounds with silica.

The aim of this study was to identify the main components of the extracts from a number of orchid plants and to study their interaction with silica surface groups by using the quantum chemical method. The data on the interaction of various components from the orchids extracts with silica surface can be useful for preparation of the extracts - silica composites, possessing desirable properties.

## Experimental

### *Materials*

All reagents were obtained from commercial sources (Merck, Germany) and used without further purification.

Orchids of *Dendrobium* and *Anoectochilus* families were grown in M.M. Gryshko National Botanic Garden of National Academy of Sciences of Ukraine under greenhouse and *in vitro* conditions. In order to grow plants *in vitro*, sterilized seeds were placed in glass flasks containing Murashige and Skoog (MS) basal medium [21] and exposed to artificial light for 16 hours per day. The list of plants used for the extracts preparation is given in Table 1.

*Table 1*

**The list of orchids used for extracts preparation.**

| *The name of taxon* | *Growing conditions* |
|---|---|
| *Dendrobium chrysanthum* Wall. Ex Lindl. | greenhouse, *in vitro* |
| *Dendrobium draconis* Rchb.f. | greenhouse, *in vitro* |
| *Dendrobium henryi* Schltr. | *in vitro* |
| *Dendrobium linguella* Rchb.f. | greenhouse, *in vitro* |
| *Dendrobium lomatochilum* Seidenf. | greenhouse, *in vitro* |
| *Dendrobium moniliforme* (L.) Sw. | greenhouse, *in vitro* |
| *Dendrobium nobile* Lindl. | greenhouse, *in vitro* |
| *Dendrobium parishii* Rchb.f. | greenhouse |
| *Anoectochilus roxburghii* (Wall.) Lindl. | *in vitro* |
| *Anoectochilus formosanus* Hayata | *in vitro* |

*Extracts preparation procedure*: 100 mL of 70% ethanol were added to 1 g of finely chopped leaves, after that the mixtures were placed into steam bath for 30 min. After cooling, the extracts were adjusted to the initial volume and filtered.

### *Methods*

*High performance liquid chromatography (HPLC)* was used for the identification and quantification of bioactive substances available in the extracts. The analysis was performed using a modular HPLC system, Agilent 1100 series (Germany) consisting of quaternary pump, autosampler, column thermostat, DAD detector. HPLC separations were achieved by using a reverse-phase Zorbax Eclipse PLUS C18 column 2.1×150 mm, 3.5 μm. Column temperature was controlled at 20°C.

Gradient elution was employed with a mobile phase consisting of 50 mM $H_3PO_4$ (solution A) and methanol (solution B) as follows: isocratic elution 89% A÷11% B with flow rate 0.2 mL/min, 0÷3 min; linear gradient from 89% A÷11% B to 34% A÷66% B with flow rate 0.2 mL/min, 3÷33 min; linear gradient from 34% A÷66% B to 0% A÷100% B with flow rate 0.2 mL/min, 33÷53 min; isocratic elution 0% A÷100% B with linear gradient of flow rate from 0.2 to 0.5 mL/min and column heating to 40°C, 53÷60 min; isocratic elution 0% A÷100% B with linear gradient of flow rate from 0.5 to 1.0 mL/min, 60÷70 min.

The analytical data were evaluated using the HP 3D Chem Station software. Wavelengths used for the identification of plant secondary metabolites, with the diode-array detector were set at 206 nm for hydroxybenzoic acids; 300 nm for hydroxycinnamic acids; 350 nm for flavonoids and their glycosides. For more reliable identification of the extracts components, their spectra and retention time were compared with those of the standard compounds: gallic, salicylic, vanillic, *p*-hydroxybenzoic, protocatechuic, syringic, *α*-resorcylic, *β*-resorcylic, *γ*-resorcylic, cinnamic, *p*-coumaric, *m*-coumaric, *o*-coumaric, caffeic, ferulic, sinapic, feruloylquinic, chlorogenic, fertaric acids, apingenin, myricetin, quercetin, quercetin 3-*O*-glucoside, kaempferol, kaempferol 3-*O*-arabinoside, kaempferol 3-*O*-glucoside. To estimate the quantity of compounds from various classes, the areas of appropriate signals were compared with those of reference substances (quercetin-3-arabinoside for flavonoids, caffeic acid for hydroxycinnamic acids and gallic acid for hydroxybenzoic acids).

Qualitative analysis of extracts composition was also performed by *laser desorption/ionization time-of-flight mass spectrometry (LDI-MS)*. Mass spectra were recorded in the positive and negative ion extraction mode on an Autoflex II mass

spectrometer (Bruker Daltonics Inc., Germany) equipped with a nitrogen laser (337 nm). The samples were ionized in the pulse mode: 3 ns pulse length, 20 Hz frequency, 65 mJ maximum energy. Spectra were recorded in the reflection mode using a delayed extraction of 20 ns and accelerating voltage 20 keV.

*Quantum chemical calculations* for individual components of the extracts and their complexes with silica clusters consisting of 12 $SiO_{4/2}$ tetrahedrons were carried out using density functional theory (DFT) method with hybrid functional $\omega$B97X-D [22] (labelled as wB97XD in Gaussian 09) with the 6-31G (d,p) basis set and the Gaussian 09 program suit [23]. Geometry was optimized using the PM6 method. The solvation effects were analysed using the solvation method SMD [24] implemented in Gaussian 09.

## Results and discussion

### *Chromatographic analysis*

The chromatograms obtained by HPLC for several orchids plant extracts are presented in Figures 1-3; Table 2 gives the classes of the identified compounds. Results show that the most abundant phenol compounds in the extracts are the representatives of three classes: flavonoids and their derivatives; hydroxycinnamic acids and their derivatives; simple phenols, tannins, hydroxybenzoic acids and their derivatives.

The flavonoids are represented mainly by flavonol *O*-glycosides, flavones *O*-glycosides and flavones *C*-glycosides, although other flavonoids of non-identified structure are also available in the extracts. The total amount of flavonoids, hydroxycinnamic and hydroxybenzoic acids in various orchids was found to be in the range of 0.30÷2.30, 0.01÷0.30, 0.01÷0.10 mg per 1 g of dried leaves, respectively. In general, the plants grown under greenhouse condition are characterized by higher total phenol content than the plants grown *in vitro* [25]. Nevertheless, such plants as *Dendrobium parishii* Rchb.f., *Anoectochilus formosanus* Hayata, *Anoectochilus roxburghii* (Wall.) Lindl. were found to have very high phenol content (up to 1.60 mg/g) although being grown *in vitro*.

A more detailed study of the substances partitioned during the HPLC procedure and the comparison of their retention times and UV-Vis spectra with the standard compounds allowed us to conclude that the majority of the extracts contain feruloylquinic, chlorogenic, sinapic and fertaric acids. All the extracts were found to contain a number of flavones and flavonols in *O*- and *C*-glycoside form, with quercetin, kaempferol and apingenin being the most abundant aglycons. Several extracts appear to include also caffeic acid, epicatechin gallate, rhamnetin and/or the derivatives of these compounds. Orchids usually contain as well a significant amount of various hydroxybenzoic acids (*i.e.* gallic, protocatechuic, syringic, ellagic acids) [9,26]; the obtained HPLC data can confirm only the presence of hydroxybenzoic acids derivatives.

*Table 2*

**Classes of compounds identified in the extracts by HPLC.**

| *Legend* | *Class of compounds* |
|---|---|
| Alk | Indole alkaloids |
| AC | Anthocyanins |
| AP | Anthracene and phenanthrene derivatives |
| B | Hydroxybenzoic acids and their derivatives, simple phenols and tannins |
| C | Hydroxycinnamic acids and their derivatives |
| Co | Coumarins |
| D | Catechins |
| F | Flavonoids of non-identified structure |
| F1 | Flavonol *O*-glycosides |
| F2 | Flavon *O*-glycosides |
| FC | Flavon *C*-glycosides |
| T | Terpenoids |

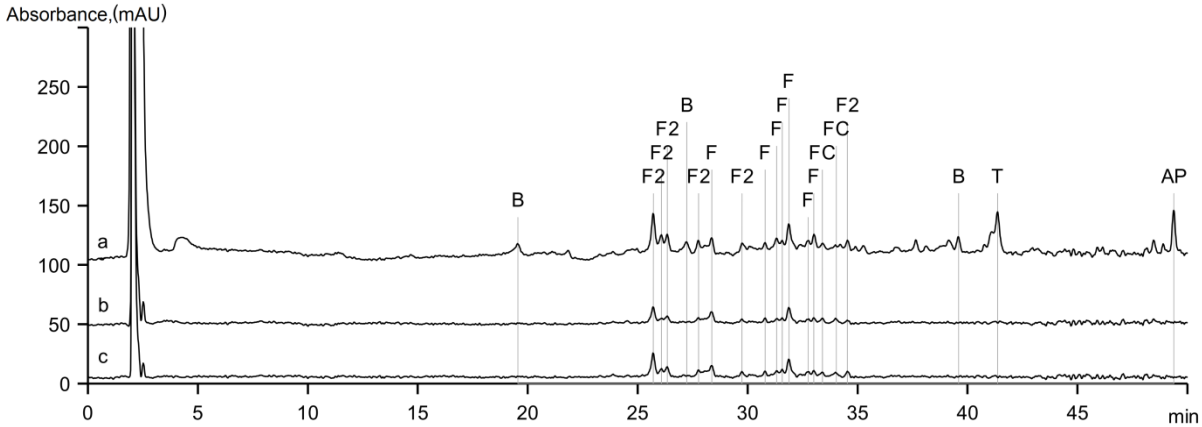



**Figure 1. Chromatograms of the *Dendrobium nobile* Lindl. extract recorded at: 206 nm *(a)*, 300 nm *(b)*, 350 nm *(c)*.**

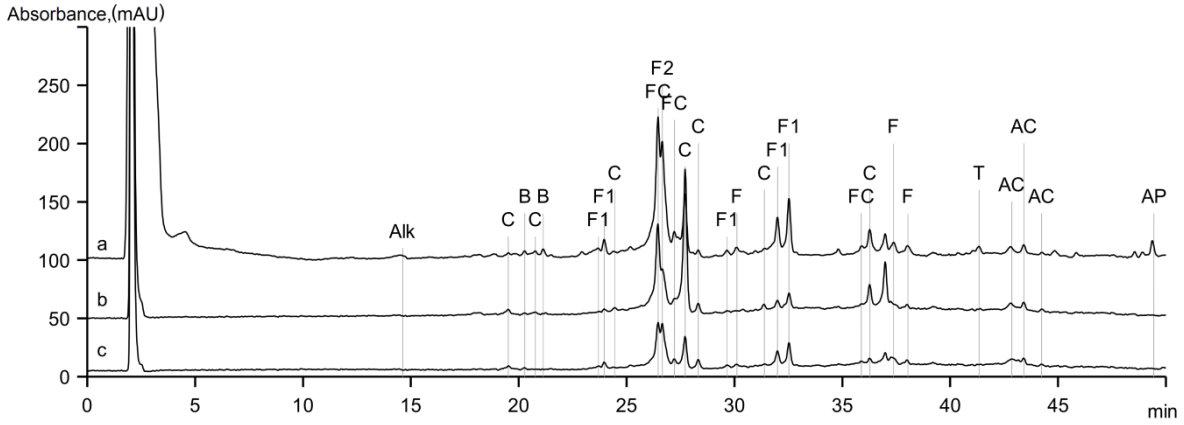



**Figure 2. Chromatograms of the *Anoectochilus formosanus* Hayata extract recorded at: 206 nm *(a)*, 300 nm *(b)*, 350 nm *(c)*.**

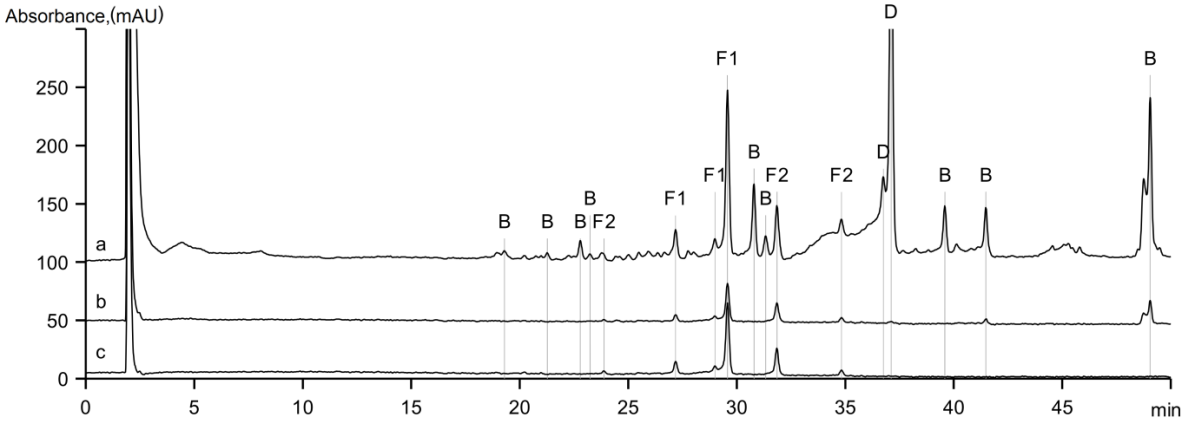



**Figure 3. Chromatograms of the *Dendrobium chrysanthum* Wall. ex Lindl. extract recorded at: 206 nm *(a)*, 300 nm *(b)*, 350 nm *(c)*.**

The mass spectroscopy data (Table 3) indicate that the extracts do contain hydroxybenzoic acids (confirmed by the signals at m/z 169 and 171 corresponding to $[M-H]^-$ and $[M+H]^+$ ions of gallic or phloroglucinic acids). The data also confirm the presence of hydrocinnamic acids or hydrocinnamic acids derivatives (the signals at m/z of 165, 225, 327, 339, 355 and 369 of $[M+H]^+$ molecular ions for coumaric, sinapic, fertaric, coumaroylquinic, chlorogenic and feruloylquinic acids). Several spectra showed peaks at m/z of 305 and 441 corresponding to $[M+H]^+$ ion of moscatilin and $[M-H]^-$ ion of epicatechin gallate, respectively. Spectra also included signals of a number of flavones or flavones derivatives (luteolin, nobiletin, apigenin and derivatives) and flavonols or flavonols derivatives (quercetin, rhamnetin, rhamnazin, kaempferol and derivatives).

***Quantum chemical calculations***

Taking into account these HPLC and LDI-MS results as well as the literature data on the orchids plants extracts composition [6], the following representatives of phenols were chosen as model compounds for the quantum-chemical study (Table 4).

All the studied compounds were found to interact with silica mainly due to the formation of hydrogen bonds between hydroxyl groups of the phenols and silanol groups of the surface. For each of the phenols, it was found that hydroxyl groups of the phenol ring formed more thermodynamically favourable complexes with silanols than others hydroxyl groups of the compounds. In the case of flavonoids, the hydroxyl groups of side B-ring form stronger complexes than hydroxyl groups of conjugated A- and C- rings. The optimized configurations of the H-bonded adsorption complexes on silica surface for various components of the extracts are given in Figure S1 (see Supplementary Material). The corresponding values of the Gibbs free energy of adsorption ($\Delta G$) and the length of H-bonds ($R_{H\text{-}bond}$) are presented in Table 4.

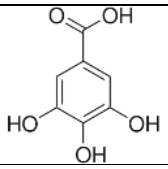
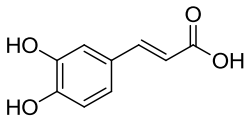
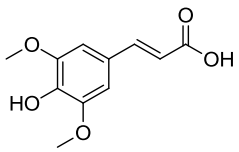
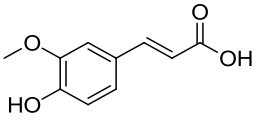
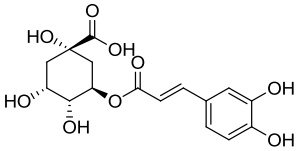
*Table 3*

**Main phenolic compounds identified in the extracts by LDI-MS.**

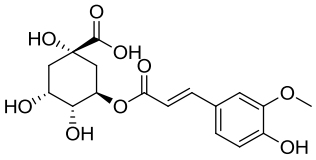
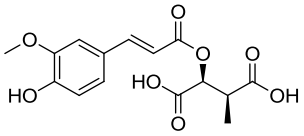
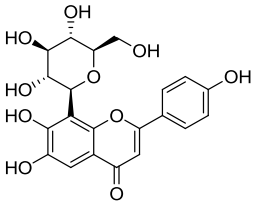
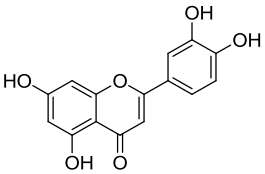
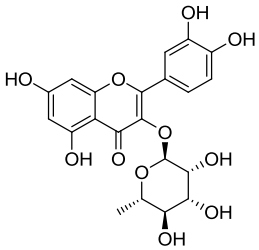
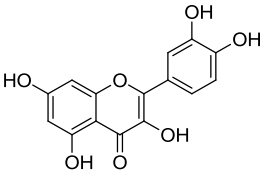
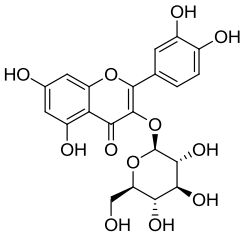
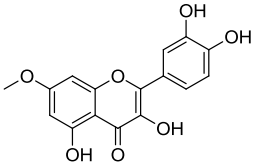
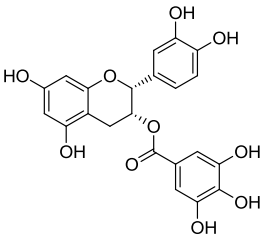
| *Class of compounds* | *Identified compound and its molecular mass, Da* | *Ions, m/z* |
|---|---|---|
| Hydroxybenzoic acids and their derivatives | Gallic/Phloroglucinic acid, 170 | $[M+H]^+$, 171<br>$[M-H]^-$, 169 |
| Hydrocinnamic acids and their derivatives | Coumaric acid, 164 | $[M+H]^+$, 165 |
| | Sinapic acid, 224 | $[M+H]^+$, 225 |
| | Fertaric acid, 326 | $[M+H]^+$, 327 |
| | Coumaroylquinic acid, 338 | $[M+H]^+$, 339 |
| | Chlorogenic acid, 354 | $[M+H]^+$, 355;<br>$[M-H]^-$, 353; $[M-H-\text{caffeoyl}-H_2O]^-$, 173 |
| | Feruloylquinic acid, 368 | $[M+H]^+$, 369;<br>$[M+H-192]^+$, 177 |
| Flavones and their derivatives | Flavon, 222 | $[M+H]^+$, 223 |
| | Luteolin, 286 | $[M+H]^+$, 287;<br>$[M+H-H_2O-2CO]^+$, 213 |
| | Nobiletin, 402 | $[M+H]^+$,403 |
| | Apigenin-7-*O*-glucoside, 432 | $[M-H]^-$, 431 |
| Flavonols and their derivatives | Quercetin, 302 | $[M+H]^+$, 303;<br>$[M+H-H_2O-3CO]^+$, 201 |
| | Rhamnetin / Isorhamnetin, 316 | $[M-H]^-$, 315 |
| | Rhamnazin, 330 | $[M+H]^+$, 331 |
| | 8-Methoxyquercetin, 332 | $[M+H]^+$, 333 |
| | Kaempferol-3-*O*-rhamnoside, 432 | $[M-H]^-$, 431 |
| Other phenols | Moscatilin (dendrophenol), 304 | $[M+H]^+$, 305 |
| | Epicatechin gallate, 442 | $[M-H]^-$, 441 |

*Table 4*

**Chemical structure of the phenolic compounds, energetic and structural parameters of the most favourable adsorption complexes of the phenols on silica surface.**

| *Class of compounds* | *Compound* | *Chemical structure* | *-ΔG, kJ/mol* | $R_{H\text{-}bonds}$, *nm* |
|---|---|---|---|---|
| Hydroxybenzoic acids and their derivatives | Gallic acid |  | 36 | 0.173, 0.186 |
| Hydroxycinnamic acids and their derivatives | Caffeic acid |  | 46 | 0.176, 0.177 |
| | Sinapic acid |  | 23 | 0.176 |
| | Ferulic acid |  | 6 | 0.277 |
| | Chlorogenic acid |  | 43 | 0.176, 0.176 |

*Continuation of Table 4*

| *Class of compounds* | *Compound* | *Chemical structure* | *-ΔG, kJ/mol* | *$R_{H\text{-}bonds}$, nm* |
|---|---|---|---|---|
| Hydroxycinnamic acids and their derivatives | Feruloylquinic acid |  | 12 | 0.283 |
| | Fertaric acid |  | 14 | 0.283 |
| Flavones and their derivatives | Apigenin-8-*C*-glucoside |  | 21 | 0.174, 0.261 |
| | Luteolin |  | 46 | 0.176, 0.177 |
| Flavonols and their derivatives | Kaempferol-3-*O*-rhamnoside |  | 18 | 0.242, 0.242 |
| | Quercetin |  | 46 | 0.176, 0.177 |
| | Quercetin-3-*O*-glucoside |  | 45 | 0.176, 0.176 |
| | Rhamnetin |  | 41 | 0.176, 0.177 |
| Other phenols | Epicatechin gallate |  | 54 | 0.175, 0.204 |

Results of this study show that various phenols significantly differ from each other by their interaction with silica. The weakest interaction with silica surface is observed for ferullic, feruloylquinic and fertaric acids (Gibbs free energy $\Delta G$= -6÷14 kJ/mol). These compounds form a single bond with surface silanols with the bond length of 0.277÷0.283 nm. Flavonoids apingenin and kaempferol interact with silica through two H-bonds and are characterized by the higher $\Delta G$ values (-18÷21 kJ/mol). Such compounds as caffeic and chlorogenic acids, quercetin, rhamnetin, luteolin, epicatechin gallate were found to have the strongest interaction with silanol groups, with $\Delta G$ and $R_{H\text{-}bond}$ values being in the range of -41÷54 kJ/mol and 0.176÷0.204 nm, respectively. The common feature of the structure of these compounds is the presence of two neighbouring hydroxyl groups in the phenol ring of hydroxycinnamic acids or in B-ring of flavonoids. Other hydroxyl groups of the phenols were found to form longer and weaker H-bonds.

For various phenols, the charges on O- and H-atoms participating in the formation of H-bonds with silanol groups did not significantly differ from each other. Thus, the steric effects seem to be the main factor affecting the interaction of various phenols with silica surface.

As it was mentioned above, flavonoids are usually available in plants in the glycoside form. The $\Delta G$ and $R_{H\text{-}bond}$ data for two variants of adsorption of kaempferol glycoside on silica surface (*via* aglycon and *via* glycoside) show that the silica-aglycon interaction is more favourable ($\Delta G$= -18 kJ/mol) than the silica-glycoside interaction ($\Delta G$= -4 kJ/mol). For adsorption of quercetin and quercetin-3-*O*-glucoside, the appropriate $\Delta G$ and $R_{H\text{-}bond}$ values are close to each other, that is, the presence of glycoside do not strongly affect the silica-aglycon interaction.

## Conclusions

Composition of sixteen plant extracts from orchid leaves was investigated by means of high performance liquid chromatography and laser desorption / ionization mass spectrometry methods. Hydroxycinnamic and hydroxybenzoic acids, as well as flavonoids in *O*- and *C*- glycosides forms were found to be the main groups of bioactive compounds of the extracts. The most common substances found in the extracts included feruloylquinic, chlorogenic, sinapic and fertaric acids and quercetin, kaempferol and apingenin in the glycoside form, while several extracts also contained gallic, coumaric and caffeic acids, luteolin, nobiletin, moscatilin, rhamnetin, rhamnazin and epicatechin gallate.

The interactions between the extracts components and silica were studied using the quantum chemical method. The adsorption of phenolic compounds on silica surface was shown to occur mainly due to the formation of hydrogen bonds between hydroxyl groups of the phenols and silanol groups of the surface, with the strength of the interaction increasing in the following order: ferullic, feruloylquinic and fertaric acids (Gibbs free energy $\Delta G$= -6÷14 kJ/mol) < kaempferol, apingenin ($\Delta G$= -18÷21 kJ/mol) << chlorogenic and caffeic acids, rhamnetin, quercetin, luteolin, epicatechin gallate ($\Delta G$= -41÷54 kJ/mol). The presence of two neighbouring hydroxyl groups in the phenol ring of the molecules was found to be a common feature in the structure of the compounds, which are characterized by the strongest interaction with silica silanol groups. These groups were shown to form the shortest hydrogen bonds lengths with silanol groups, providing the compounds with a strong interaction with silica surface.

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## Supplementary information

Supplementary data are available free of charge at http://cjm.asm.md as PDF file.

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