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Mechanochemical Interaction of Quercetin and Glucose. Detecting Glycoside Bond in IR Spectra

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Abstract

Reactions of quercetin and carbohydrates produce different compounds. IR spectroscopy detects glycoside bond formation. The reaction for the synthesis of glycosides in solution is labour-consuming and costly in time and resources. Nevertheless, reaction progress becomes easier in the solid phase. An opportunity to generate glycosides during mechanochemical activation of a mixture of solid quercetin and glucose significantly simplifies and cheapens some technologies in the food industry and feed preparation. IR spectra of quercetin, glucose, and isoquercitrin were acquired by quantum chemical modeling (Gaussian 09) in the initial step. They were then obtained experimentally for reagents and possible reaction products (Tensor 27, Bruker). New absorption bands were detected in IR spectra. Absorption bands in the 950–1050 cm^{-1} region are typical for the formation of a glycoside bond from carbohydrate and aglycone and may be assigned to the natural glycoside isoquercitrin.

Key words: glycoside bond, quercetin, glucose, IR spectrum, quantum chemical modeling, mechanochemical activation

INTRODUCTION

Flavonoids and their water-soluble glycosides have biological activity. Their synthesis by the interaction of polyphenol quercetin with carbohydrate glucose in solution is labour-consuming and costly in time and resources. Glycoside formation from insoluble bioflavonoids from vegetable raw materials during mechanochemical extraction processes substantially broadens the application range of flavonoid drugs, enhances the environmental purity and manufacturability [1]. Reducing labour costs for the manufacture of the drugs is likely to expand the scope of bioflavonoids. Apart from the pharmacy, they may be used in functional nutrition, veterinary medicine, and forage production, which does not require the selection and thorough treatment of glycosides.

As demonstrated in [2], quercetin-3-O- β -D-glucopyranoside known as isoquercitrin in nature is generated in the reaction of quercetin and glucose.

The aim of the research was to demonstrate an opportunity to obtain a glycoside during mechanochemical activation of quercetin and glucose, and also to prove glycoside bond formation by IR spectroscopic data.

EXPERIMENTAL

Commercial reagents, such as glucose (crystalline glucose, GOST 975–88, Khimreaktiv), quercetin (Diam), and isoquercitrin (AppliChem), were selected for comparison purposes and as initial compounds. The mechanical processing of a mixture of glucose and quercetin powders was

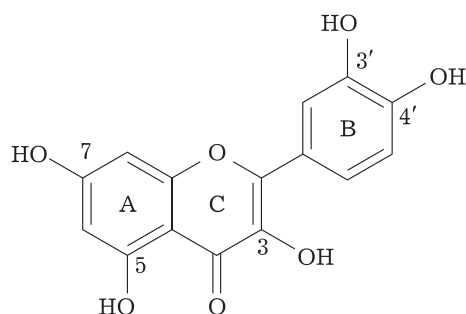


Fig. 1. Quercetin.

carried out in an AGO-2 activator; 1 W/g mode (the acceleration of the impacting bodies (balls) is 200 m/s^2); SHH15 stainless steel balls, 5 mm in diameter; loading balls is 200 g, the mass ratio of loading balls to processed powder mixture sample is 20 : 1.

IR spectra were simulated quantum-chemically in Gaussian 09 (B3LYP/6-31G*, Siberian SuperComputer Centre of the Siberian Branch of the Russian Academy of Sciences) and experimentally acquired using a Tensor 27 device (Bruker) in KBr (Centre for Collective Use, N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry).

RESULTS AND DISCUSSION

Quercetin (Fig. 1), 3,3',4',5,7-pentahydroxyflavone, $\text{C}_{15}\text{H}_{10}\text{O}_7$. The molar mass is 302 Da. The formula is presented by three rings, *i.e.* A, C, and attached ring B. In total, a molecule of quercetin is comprised of five hydroxy groups. Quercetin may react with different compounds either at one or several OH groups. It acts as aglycone upon interacting with hydrocarbons. It is believed that binding with hydrocarbons *via* a glycosidic carbon atom (Fig. 2, position 1) of sugar is most frequently met.

D-glucose is the most thermodynamically stable hexose. Glucose (*D*-glucopyranose) is present-

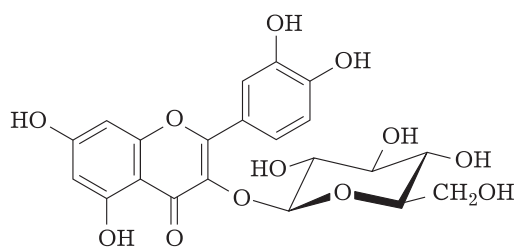


Fig. 3. Isoquercitrin.

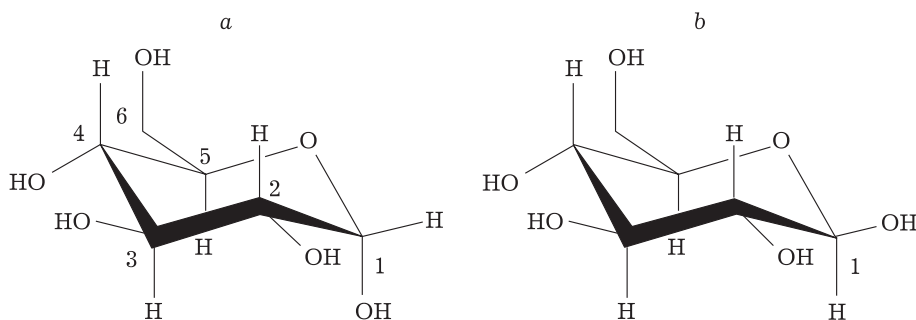
ed in the natural state by the cyclic form, α - and β -anomers (see Fig. 2); the general formula is $\text{C}_6\text{H}_{12}\text{O}_6$, $M = 180 \text{ Da}$. There is an equilibrium between these forms due to mutarotation; the number of other forms is insignificant. The ${}^4\text{C}_1$ chair conformer is more stable.

Figure 2 presents α - and β -*D*-glucopyranose molecules. They differ in the position of the glycosidic hydroxyl at the C1 atom: in α -anomer, this group is perpendicular to the plane of the ring (axially), in the β -anomer – in the plane; all hydroxyl groups are equatorially located.

Each reagent under consideration has five active hydroxyl groups. Twenty five isomers for each anomer are likely to form upon the interaction of quercetin and *D*-glucopyranose. As demonstrated by the performed modeling of structures using molecular mechanics [2], the glycoside formed *via* the oxygen bridge atom and the carbon one in the third position of a molecule of quercetin bonded to the carbon atom in β -*D*-glucopyranoside is most thermodynamically favourable. This compound is known as the natural glycoside isoquercitrin. Isoquercitrin (Fig. 3), quercitrine-3-O- β -*D*-glucopyranoside, $\text{C}_{21}\text{H}_{20}\text{O}_{12}$, $M = 464 \text{ Da}$.

IR spectra were acquired by quantum chemical modelling for the selected compounds (reagents quercetin and β -*D*-glucopyranoside, a possible product is isoquercitrin).

Research work [3] modelled IR spectra of various flavonoids. The region of C–O–H stretching vibrations responsible for the further formation,

Fig. 2. α - (a) and β - (b) -*D*-glucopyranose.

e. g., glycosides, for quercetin is in the 1100 cm^{-1} range. The quantum chemical modeling of the IR spectrum in [3] was carried out by AM1 semi-empirical method.

On the other side, it is known [4] that absorption bands in the $950\text{--}1050\text{ cm}^{-1}$ range are considered to be a typical feature of a glycoside bond. In case of anomers, the presence of the glycosidic hydroxide of sugars in the β -position causes the absorption shift towards higher frequencies.

Figures 4 and 5 give the resulting model spectra of quercetin, glucose, and isoquercitrin. It can be seen that for the initial compounds (quercetin and glucose), the peaks are absent in this fre-

quency range, whereas there is absorption for isoquercitrin. Identification ranges of $950\text{--}1100\text{ cm}^{-1}$ may be selected for the model spectrum of isoquercitrin. For example, the band near 1106 cm^{-1} corresponds to complex vibrations that involve asymmetric stretching vibrations of C3 (quercetin)-O (glycoside)-C1 (the glucopyranose ring).

Figure 6 provides IR transmittance spectra of reference compounds (quercetin, glucose, and isoquercitrin) and a sample of a mixture of quercetin and glucose produced resulting from mechanical activation. In order to identify the glycoside bond, the $950\text{--}1100\text{ cm}^{-1}$ range was also selected. Unlike initial quercetin and glucose,

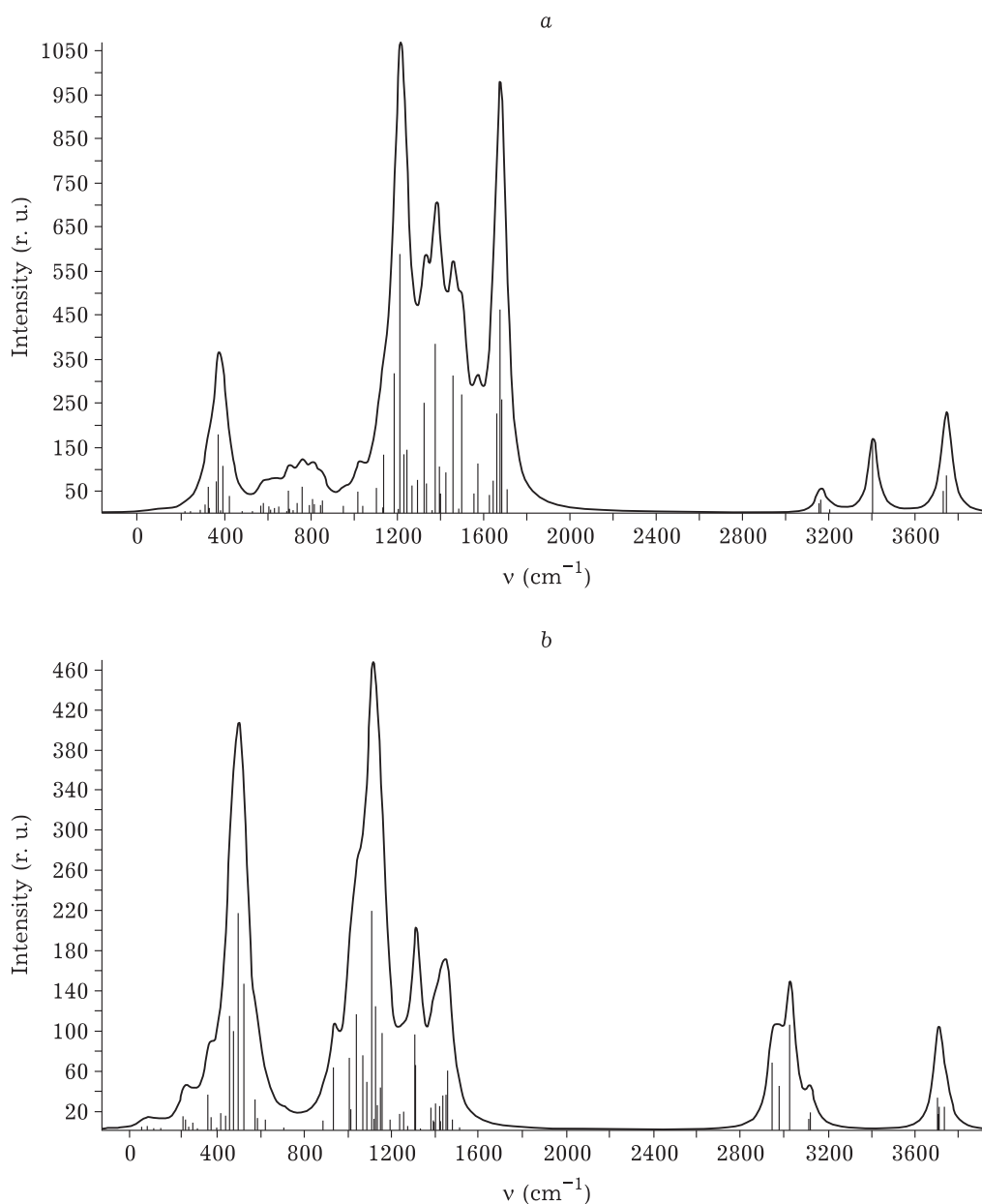


Fig. 4. Model absorption spectra of quercetin (a) and β -D-glucopyranose (b).

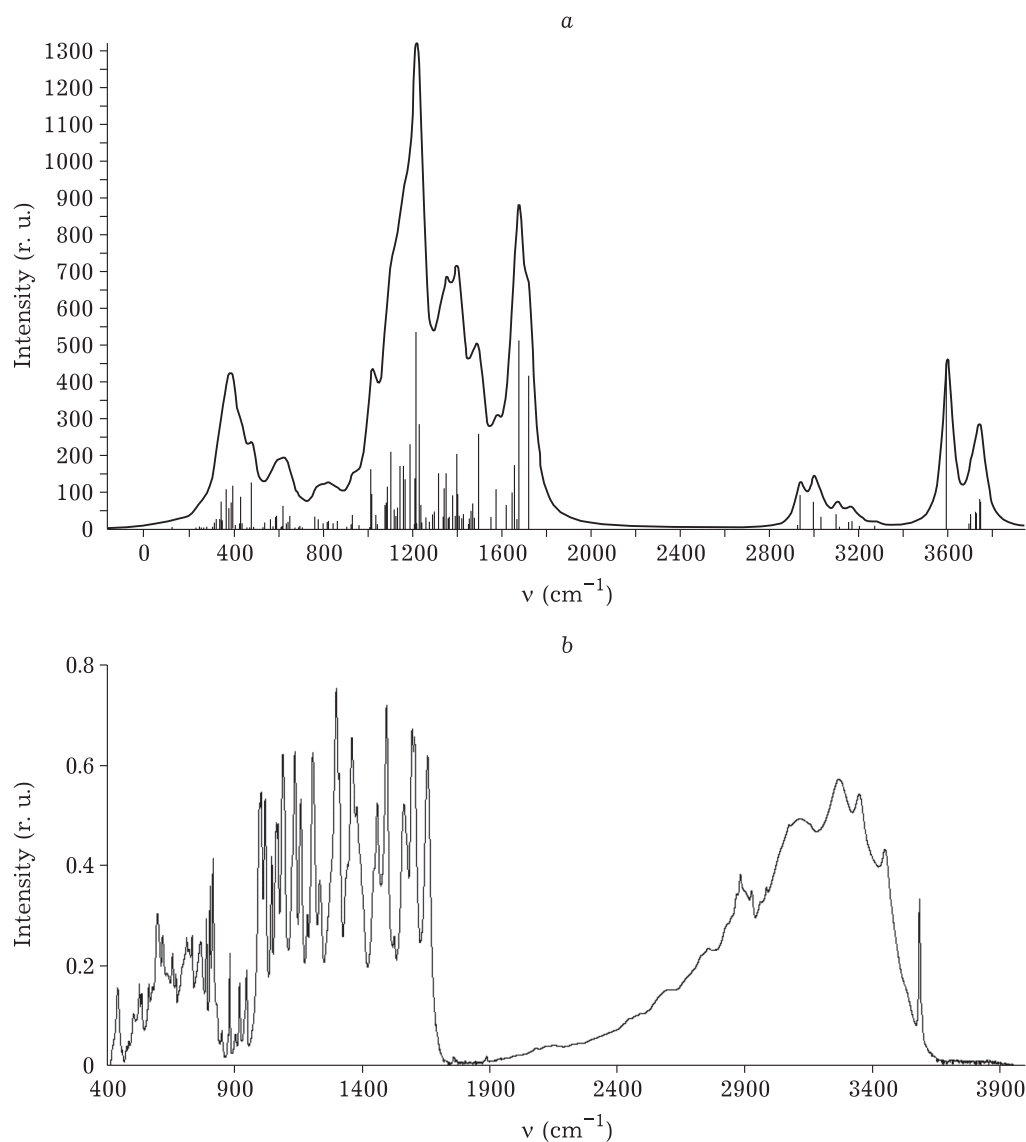


Fig. 5. Model absorption spectra of quercetin (a) and β-D-glucopyranose (b).

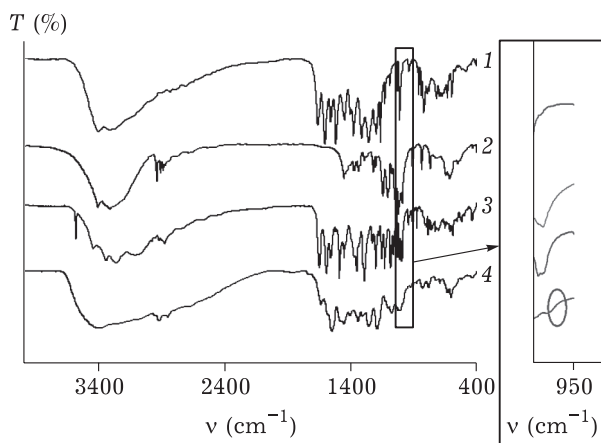


Fig. 6. Experimental IR spectra of samples: 1 - quercetin, 2 - glucose, 3 - isoquercitrin, 4 - mechanoactivated mixture of quercetin and glucose. The highlighted section of the spectrum is shown in the insert.

the appearance of absorption bands similar in the position to the reference compound, *i.e.* isoquercitrin, is latched in the insert. They indicate glycoside formation and glucose produced during mechanochemical activation.

CONCLUSION

1. The quantum-chemical modeling of IR spectra of quercetin, glucose, and isoquercitrin was carried out. Absorption frequencies corresponding to vibrations of a glycoside bond formed in the place of attaching a hydrocarbon (glucose) to aglycone (quercetin) were determined.

2. Reference frequencies of 950–1100 cm⁻¹ were selected for further research on the formation reaction of glycosides and comparison of model and

reference (experimental) IR spectra of quercetin, glucose, and isoquercitrin was carried out. Reference absorption frequencies of stretching vibrations of glycoside bond are present in the spectrum of isoquercitrin but are absent in spectra of reagents.

3. Mechanochemical interaction of glucose and quercetin was carried out experimentally. The appearance of reference frequencies was noted in the spectra of the product. On this basis, a conclusion was made regarding the flowing of the glycosylation reaction upon the mechanical processing of a mixture of quercetin and glucose powders.

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