Investigation of glycation products by THz time-domain spectroscopy

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***Abstract*— Glycation is the non-enzymatic reaction between reducing sugars, such as glucose, and proteins, lipids or nucleic acids. This process involvement in various pathologies of the human body, including diabetes and aging, and is an intensive field of research. Terahertz time-domain spectroscopy (THz-TDS) has been used for assay of glycation products. The transmission and the attenuated total internal reflection geometries have been used for measuring of a number glycation products in aqueous solutions at 0.2-2.5 THz.**

I. INTRODUCTION

Among the diseases associated with metabolic disorder, the most costs society bears from diabetes mellitus (DM) and its complications. Diabetes is characterized by high levels of blood glucose. Earlier detection of DM and control the degree of compensation recommended the determination of glucose in blood. Then it was found more evident correlation between the presence of vascular complications of diabetes and the degree of progression was observed with the level of glycated hemoglobin and other glycated proteins. Protein glycation is a non-enzymatic reaction between the carbonyl groups of monosaccharides such as glucose and fructose with the amino groups of proteins.Glycation leads to formation of advanced glycation end-products (AGEs) [1]. Glycation is a main cause of spontaneous damage to the structure of intracellular and extracellular proteins. In diabetes mellitus, glycation is more active, and therefore, can be regarded as a factor that contributes to the chronic pathology [1, 2]. AGEs are formed after several hours of high glucose concentrations in blood. In addition to circulation in the blood AGEs accumulate in tissues and skin.

Quantitative analysis of glycation products from a technical point of view is a serious problem, and is solved by invasive methods. The most accurate method for their quantitative determination is chromatography with mass spectrometric detection. Fluorescence spectroscopy is using for control of AGEs accumulation. For example, fluorescence spectra of blood plasma at 320 nm excitation, which connected with AGEs formation, have been measured [3]. But the numbers of AGEs have no fluorescence. Among non-fluorescent AGEs, there are N-(carboxymethyl)lysine, glyoxal or imidazolone [3].

THz spectroscopy is additional tool for glycation products control. For example, the THz absorption of blood plasma was shown earlier to be significantly reduced, depending on the diabetes severity [4]. We used the transmission THz spectroscopy to study an early stage of albumin glycation. BSA was incubated with reducing sugars during 96 h. It was demonstrated that an averaged transmission coefficient is diminished during incubation of BSA with sugars [5]. We consider that glycation of BSA results in a change the parameters of slow Debye relaxation.

In this report, we study the early stage glycation products and AGEs, such as pentosidine, glyoxal and others and determine their contribution to the absorption in THz range. The work will discuss experimental and theoretical study of the absorption spectra of glycation products.

II. RESULTS

Used THz-TDS spectrometers were described previously [5, 6]. Incubation of proteins with sugars was performed according to the method described in [5]. It was studied dry substances and solutions. Dry substances were measured in a specially designed cuvette (Fig.1). The cuvette has a 3 mm thick area with a transparent window for measurements.

Fig. 1. Cuvette for measuring of the absorption of dry substances

Terahertz radiation was transmitted through this window, 16 corresponding signals were obtained for 16 various spatial points and averaged. The space-averaged signal in the frequency region is shown in figure 2. Preliminary, an empty cell was scanned in the same way, for which 16 reference signals were also measured.

Also the special cuvette was created to study solutions (Fig.3). A solution was placed into the cuvette and spatial scanning was carried out. The cuvette has a dedicated measurement part (part "b"), which provides a solution thickness of 1 mm. The cuvette lower part " C " is separated by a partition and is designed to obtain a reference signal.

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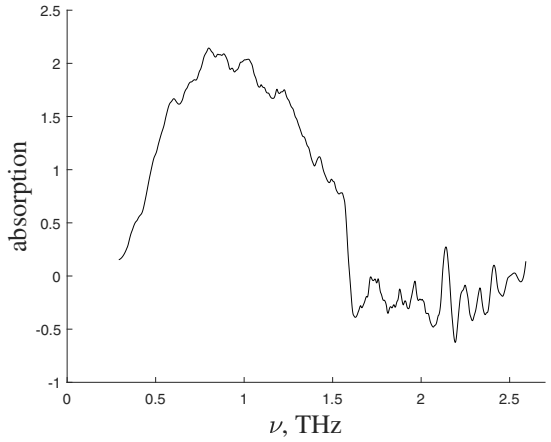

Fig. 2. Imidazole THz absorption spectrum

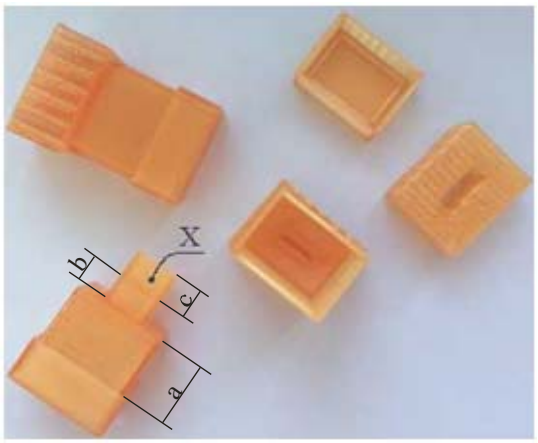

Fig. 3. Cuvette for measuring of solution absorption

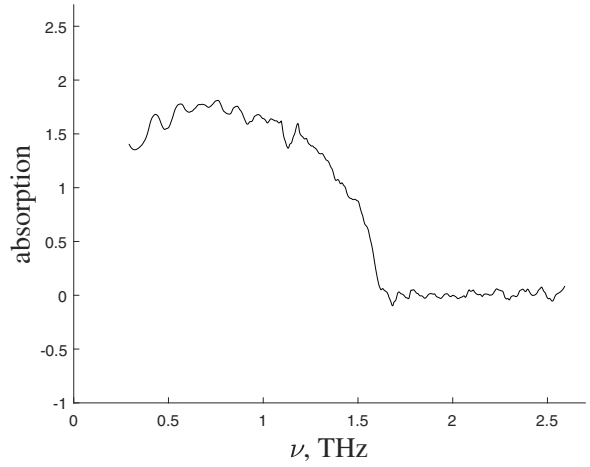

Fig. 4. The THz absorption spectrum of glyoxal (40%, aqueous solution)

III. CONCLUSION

Preliminary study of optical properties of early stage glycation products and AGEs in THz range has been carried out. Some specificity was shown to be for THz absorption spectra of dry substances and solutions. Our results can be used for future analysis of AGE in biotissues.

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