SCIENTIFIC CONTRIBUTIONS

Chief Assistant Professor Veronika Atanassova Karadjova
for participation in the contest for the academic position of "Associate Professor" in the field of
higher education 4. Natural Sciences, mathematic and informatics, professional field
4.2. Chemical Sciences, scientific specialty Inorganic Chemistry
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Reference for scientific contributions was made on the basis of **27 scientific publications** applied in the contest for academic position of Associate Professor, where 23 articles are indexed in **SCOPUS** and **Web of Sciences** databases with Impact Factor or SJR and 4 articles are in non-indexed journal with peer-review.

The citation list contains 32 citations.

The scientific results have been presented at 38 national and international scientific symposiums and conferences as **29** posters and **5** oral presentations.

In the context of the abovementioned results the Hirsh index in accordance with the records in Scopus is **4**.

A part of the scientific results are outcomes of 5 national projects (in 3 of them the applicant is a member of the team, while in 2 project is the Principle Investigator), 8 projects financed by the Scientific Investigation Sector of UCTM (Principle Investigator) and 1 project governed by South-West University „Neophit Rilski (team member).

The main experimental results and contributions can be presented in several directions, among them (the numbers are in accordance with the main list of scientific publications):

A. Synthesis, Structure and properties of Beryllium salts

A. 1. Investigation of crystallization processes in triple aqueous systems of beryllium salts and determination of diagrams of solubility.

A. 2. Characteristics of double beryllium salts by means of X-ray powder diffraction and single-crystal diffraction.

A. 3. Infrared spectroscopic studies of double beryllium salts and correlations between the infrared spectra and the observed crystal structures, and factor group analysis.

A. 3. 1. Analysis of normal vibrations of water molecules and anionic structural motives

A. 3. 2. Analysis of the Анализ на hardness of the hydrogen bounds in beryllium compounds by means of a matrix infrared spectroscopy (method of isotopic dissolution and matrix isolated HDO molecules)

B. Synthesis, Structure and properties of Tuton salts

B. 1. Investigation of crystallization processes in aqueous salt systems: M'_2XO_4–$M''XO_4$–H_2O *(M' = Rb, Cs; M'' = Mg, Co, Ni, Cu, Zn). Solubility diagrams*

B. 2. Characteristics of Tuton salts by X-ray powder diffraction

B. 3. Infrared spectroscopic studies of double salts and correlations between the crystal structure and the infrared spectra. Factor group analysis

B. 3. 1. Analysis of normal vibrations of sulphate and selenite ions

B. 3. 2. Assessments of the stability of hydrogen bonds in the salts of Tuton type

B. 3. 3. Investigation of vibration behavior of matrix-isolated SO_4^{2-} *ions in selenate matrices and of* NH_4^+ *ions, matrix isolated in selenite and sulphate matrices. Degrees of energetic deformation of matrix isolated ions.*

B. 3. 4. Analysis of libration vibrations of water molecules in mixed crystals

C. Synthesis and studies of bio-active substances

C. 1. Synthesis and investigations of peptide based structures

C. 2. Synthesis and investigations of phenolic compounds

C. 3. Application of the structural analysis's method for investigations of bio-active substances and materials

A. Synthesis, structures, and properties of Beryllium salts (publications 1A, 2B, 4B, 12B, 13A, 14A)

The chemistry of Beryllium and its compounds is of great interest due to the possibility of their applications in some high technologies. In addition, the beryllium compounds are characterized by strong biological activities. The perspectives in these directions address the nuclear physics and energetics (as nuclear fuel), aviation elements, missile propulsions, satellite structures, space stations, communication and navigation systems, defense applications, computer elements (as connectors), audio components, high-efficiency thermal elements, fuel cells, geological and oil and gas production equipment. The Beryllium compounds are elements of high-technological ceramics, microwave ovens, and additives to plastics and glasses.

A. 1. Studies of crystallization processes in triple aqueous systems with beryllium salts. Solubility diagrams

The study of the solubility in three-component aqueous systems of salts allows the determination of the crystallization fields of the equilibrium solid phases and to define graphically their contents by the Schreinemakers method. The equilibria between solid and liquid phases have been attained by the method of isothermal monitoring of the saturation. The classical analytical methods (complexometric techniques and sedimentation weighing method) were used to determination of the contents of the liquid phases and their equilibrium wet solid phases.

- Applying physico-chemical analysis it was possible to study the solubility of 9 three-component systems (at 25ºC) with the participation of beryllium selenate and beryllium iodate, namely:

$BeSeO_4 – (NH_4)_2SeO_4 – H_2O$

$BeSeO_4 – MeSeO_4 – H_2O$ (Me = Co, Ni, Zn, Cu)

$MIO_3–Be(IO_3)_2–H_2O$ (M = K, NH_4^+, Rb, Cs)

The developed solubility diagrams allow the crystallization fields of the equilibrium solid phases to be determined.

It was determined that for systems such as $BeSeO_4 – MeSeO_4 – H_2O$ (Me = Co, Ni, Zn, Cu) are from the simple eutectic type and only crystallization fields of simple salts, i.e. $BeSeO_4·4H_2O$ и $MeSeO_4·6H_2O$ (Co, Ni, Zn) and $CuSeO_4·5H_2O$ were observed. The wide of the simple salt crystallization fields is correlated to their solubilities in binary solutions.

- For the three-component system $(NH_4)_2SeO_4–BeSeO_4–H_2O$ the concentration area corresponds to equilibrium double salt with composition $(NH_4)_2Be(SeO_4)_2·2H_2O$ was determined.

As a result of the processes of complex formations in triple iodate solutions, the constructed solubility diagrams of: $MIO_3–Be(IO_3)_2–H_2O$ (M = K, NH_4^+, Rb, Cs) allowed determinations of wide concentration areas where crystallizations of double salts such as $M_2Be(IO_3)_4·2H_2O$ (M = K, NH_4^+, Rb) are possible. The system $CsIO_3–Be(IO_3)_2–H_2O$ is of a simple evtonic type (the impossibility to form a double salt can be attributed to the much larger ionic radius of the cesium ions).

As a result of the studies carried out in this direction a new beryllium compound was obtained, namely: $Rb_2Be(IO_3)_4·2H_2O$.

A. 2. Characterization of double beryllium salts by meads of X-Ray powder diffraction and X-ray diffraction of single-crystal

By means of X-ray diffraction of single-crystal the crystal structure of the double salt was defined:
$(NH_4)_2Be(SO_4)_2\cdot 2H_2O$ (article 3)
The compound crystalizes in monoclinic space group $P2_1/c$, with following parameters: a = 11.448(2), b = 11.876(2), c = 7.439(1) Å, β = 96.64(1)°, V = 1004.6 $Å^3$, Z = 4.

The powder roentgenograms treated by the codes ITO and LSUCR allow calculating the parameters of unit-cell cells of the following salts:
$(NH_4)_2Be(SeO_4)_2\cdot 2H_2O$
$M_2Be(IO_3)_4\cdot 2H_2O$ (M = K, NH_4^+, Rb)
It was discovered that $(NH_4)_2Be(SeO_4)_2\cdot 2H_2O$ crystalizes in a monoclinic space group $P2_1/c$, with the following parameters: a = 11.747(3) Å, b = 12.212(4) Å, c = 7.649(2) Å, β = 96.94(3)°, V = 1089.3(3) $Å^3$, Z = 4.

Further $(NH_4)_2Be(SeO_4)_2\cdot 2H_2O$ is isostructural with $(NH_4)_2Be(SO_4)_2\cdot 2H_2O$, as well as with corresponding potassium and rubidium selenates and sulphates (monoclinic structure). The structures of the double salts consist of fragments containing $[BeO_2(H_2O)_2]^{2+}$- tetrahedrons which share common picks with two crystallographic types XO_4^{2-} tetrahedrons (X = S, Se). These structural motives are connected to ammonia ions and hydrogen bonds in double layers, parallel to (100). In addition, the layers are connected Допълнително слоевете са свързани with NH^+_4 ions and hydrogen bonds in a 3D structure.

The structures of the corresponding ammonia salts are additionally stabilized by means of a system of hydrogen bonds formed between the formed XO_4^{2-} and NH_4^+ ions.

The double iodates $M_2Be(IO_3)_4\cdot 2H_2O$ (M = K, NH_4^+, Rb) are isostructural and crystalize in monoclinic space group $P2/m$ having parameters close to the unit-cell: $K_2Be(IO_3)_4\cdot 2H_2O$ – a = 14.218(5) Å, b = 6.747(2) Å, c = 5.765(2) Å, β = 98.74(4)°, V = 546.6(2) $Å^3$; $(NH_4)_2Be(IO_3)_4\cdot 2H_2O$ – a = 14.414(4) Å, b = 6.838(2) Å, c = 5.947(2) Å, β = 99.52(4)°, V = 578.0(2) $Å^3$; $Rb_2Be(IO_3)_4\cdot 2H_2O$ – a = 14.423(4) Å, b = 6.867(2) Å, c = 5.743(3) Å, β = 98.15(3)°, V = 562.9(3) $Å^3$.

3. Infrared spectroscopic studies of double beryllium salts. Correlations between the crystal structures and infrared spectra. Factor group analysis.

Both the infrared and Raman spectroscopies are the most applied for the characterization of chemical substances It is well-known that the vibrational spectra of solids reflect the in-body and intermolecular interactions of the molecules and ions forming the structure of a certain chemical compound and the effects of the crystal field. As a result, the spectrum becomes much more complex than that of the free molecules and ions, when they are in gaseous or solutions. These interactions make difficulties, and sometimes this impossible, in the determination of the wavenumbers of the vibrational bands of the spectra of solids.

A. 3. 1. Analysis of normal vibrations of water molecules and anionic structural motives

It was determined a correlation between the vibrational spectra (Infrared and Raman) and the structures of beryllium salts, presented by correlation diagrams. The number of vibrational bands and their wavenumbers are discussed in light of the positional symmetry of the structural motives and the strength of the chemical bonds.

The vibrational spectra of the double salts $(NH_4)_2Be(SO_4)_2{\cdot}2H_2O$ and $(NH_4)_2Be(SeO_4)_2{\cdot}2H_2O$ are discussed concerning the normal vibrations of tetrahedral ions, the hydrogen bonds strength, and the lattice vibrations of the tetrahedra BeO_4 (skeleton vibrations). It was estimated that the infrared bands in the spectrum of $(NH_4)_2Be(SO_4)_2{\cdot}2H_2O$, corresponding to the valence vibrations ν_3 and ν_1, are observed and doublets due to the existence of two crystallographic types of sulphate tetrahedra. The spectral area where the valence vibrations of the selenate ions $(NH_4)_2Be(SeO_4)_2{\cdot}2H_2O$ is significantly larger and is related to the strong internal and intermolecular interactions of these ions.

The values of $\Delta\nu_3$ and $\Delta\nu_4$ corresponding to SeO_4^{2-}, and the spectral area widths reveal that there are valence and deformation vibrations of selenate ions and therefore it might be suggested that these ions are exerted to stronger energetic, a fact that cannot be predicted based on structural data.

The standpoint concerning strong covalence bonds between Be^{2+} ions and oxygen atoms of ligand waters leads to an increase of the infrared bad intensity corresponding to the lattice vibrations of the beryllium tetrahedra (skeleton vibrations), and it is comparable with the normal vibrations of the other molecular units forming the structures of the beryllium salts.

The vibrational spectra (infrared and Raman) confirm the isostructural nature of the double salts $M_2Be(IO_3)_4{\cdot}2H_2O$ ($M = K, NH_4^+, Rb$). The widths of the spectral areas, where normal vibrations of iodate ions are observed, and the number of infrared bands corresponding to these vibrations, reveal that at least two crystallographic types of iodate ions form the structure of these double salts.

A. 3. 2. Analysis of hydrogen bonds strengths in beryllium compounds by mends of matrix infrared spectroscopy (method of isotopic dissolution; matrix-isolated HDO molecules)

The studies on the hydrogen bonds are motivated by their importance in revealing the natures and mechanisms of various chemical and biochemical processes, dimerization and polymerization processes, and properties of chemical compounds. By their nature, the hydrogen bonds are intermolecular interactions with electrostatic character and are performed in almost all solids, solutions, and liquids, where specifically bonded hydrogen in molecules or ions (proton donors), and atoms with free electrons (proton acceptors) are available. The hydrogen bonds are important for the stabilization of structures of solids and particularly the salt hydrates. The main structural methods for studies are X-Ray and neutron diffractions, vibrational spectroscopy (infrared and Raman), and nuclear magnetic resonance. Deep analyzes of the hydrogen bond nature in inorganic salts and the crystal-chemical parameters are available in the work of Lutz и Engelen [H. D. Lutz, B. Engelen, Trends Appl. Spectrosc., 4 (2002) 355, H.D. Lutz, C. Jung, J. Mol. Struct.,404, 1997, 63-66].

The hydrogen bond strengths on inorganic crystal-hydrate salts were studied by the method of isotope dissolution (matrix isolated HDO molecules) and deuterization up to 80%.

The values of the wavenumbers, corresponding to the valence vibration OD of the matrix-isolated HDO, was used to assess the hydrogen strength of double salts $(NH_4)_2Be(SO_4)_2 \cdot 2H_2O$ and $(NH_4)_2Be(SeO_4)_2 \cdot 2H_2O$ and the results were compared to the same situation in the corresponding potassium counterparts, i.e., $K_2Be(SO_4)_2 \cdot 2H_2O$ and $K_2Be(SeO_4)_2 \cdot 2H_2O$.

Ther hydrogen bonds in the ammonium salts are weaker than those in the corresponding potassium counterparts due to the weaker proton acceptor capacity of the anions in the ammonia salts, determined mainly by formations of hydrogen bonds with ammonia ions (anti-cooperative effect). The infrared spectra reveal strong interactions between water and sulphate molecules, and respectively between selenate ions and the vibration of BeO_4 tetrahedra. These interactions lead to low values of the isotope displacement of the molecule librations, values close to unity.

The infrared spectroscopic studies of $M_2Be(IO_3)_4 \cdot 2H_2O$ ($M = K, NH_4^+, Rb$) reveal that the potassium and the rubidium salts have relatively strong hydrogen bonds, a standpoint based on the wavenumber values of ν_{OD} vibrations of the matrix-isolated HDO molecules (isotopically dissoluted samples), due to strong interaction in Be-OH_2 (synergetic effect). The smaller electronic radius of the potassium ions results in stronger internal and intramolecular interactions and yields stronger hydrogen bonds in the potassium salt in contrast to the rubidium counterparts.

The hydrogen bonds, the formed water molecules, in the ammonium salt are significantly weaker than in the case of potassium and rubidium salts due to the weaker proton acceptor capacity of the iodate ions attributed to the formation of hydrogen bonds of the anions with the ammonium cations (anti-cooperative effect). The vibrations of the water molecules and the isotopic ratios $\nu_L(H_2O)/\nu_L(H_2O)$ were analyzed too. The small values of these ratios (close to unity) confirm the formation of strong hydrogen bonds in the salts investigated.

The analysis of the infrared spectra allows us to suggest that the Be^{2+} ions are coordinated with two water molecules and two different crystallographic iodate groups forming $[Be(H_2O)_2(IO_3)_2]$ tetrahedra.

The summation of the results developed on the beryllium salts, as part of the PhD thesis “Synthesis, structure and properties of beryllium sulphate and selenate salts”. The experimental results are discussed in light of the processes of complex formations in triple solutions $BeSeO_4-K_2SeO_4-H_2O$, $BeSO_4-Rb_2SO_4-H_2O$ и $BeSeO_4-MSeO_4-H_2O$ (M = Co, Ni, Cu, Zn) at 25 ºC and the solubility of the salt components in their binary solutions. As a result of processes of co-crystalization new compounds $Rb_2Be(SO_4)_2 \cdot 2H_2O$ and $K_2Be(SeO_4)_2 \cdot 2H_2O$ were obtained. The crystal structures of $BeSeO_4 \cdot 4H_2O$, $M_2Be(SO_4)_2 \cdot 2H_2O$ (M = K, Rb), и $K_2Be(SeO_4)_2 \cdot 2H_2O$ employing X-Ray diffraction of single-crystal was developed. The vibration spectra are discussed in light of the crystal structures of beryllium salts and the crystal-chemical properties of different molecules and ions. Special attention was paid to the effects of different crystal-chemical factors on the hydrogen bond strengths.

The matrix infrared spectroscopy was applied to resolve the following crystal-chemical problems:

- Distribution of SO_4^{2-} ions in two possible crystallographic positions when they are included in the structure of $K_2Be(SeO_4)_2 \cdot 2H_2O$; ions in $BeSeO_4 \cdot 4H_2O$ based on the vibrational behavior of matrix-isolated SO_4^{2-} ions;
- The strength of hydrogen bonds (method of isotope dissolution – matrix isolated HDO molecules).

B. Syntesis, structure and properties of Tuton salts (publications 3B, 15A, 16A, 17A, 24C, 25C, 26C)

In the last years, intensive studies are directed to searching for new materials with proton permeability. The hydrates of some normal and hydrogen salts such as phosphates, selenates and sulphates and hydrates of oxides, with strong acidic properties. The main motivation for studies of potassium, ammonia and rubidium Tuton salts is the possibility of these compounds exhibiting proton permeability due to the existence of strong hydrogen bonds in their strictures. Among these compounds, a special place is taken by salts with M^+ ions replaced by ammonia ions.

B. 1. Studies on the crystallization processes in triple aqueous solutions of salts: M'_2XO_4–$M''XO_4$–H_2O (M' = Rb, Cs; M'' = Mg, Co, Ni, Cu, Zn). Diagrams of solubility.

Applying the isothermic monitoring of the saturation solubilities of 12 three-component aqueous salt systems of the following type was carried out:

Rb_2SeO_4–$MSeO_4$–H_2O (M = Mg, Ni, Cu)
Rb_2SO_4–MSO_4–H_2O (M = Mg, Co, Ni, Cu, Zn)
Cs_2SO_4 – MSO_4 – H_2O (M = Mg, Co, Ni, Zn)

The solubility diagrams of the studied systems and the determined crystallization fields of the equilibrium phases were determined. Due to strong processes of complex formation in the triple saturated solutions, there are areas of double salts with large crystallization fields of double salts with a general formula $Rb_2M(XO_4)_2{\cdot}6H_2O$ (M = Mg, Co, Ni, Cu, Zn; X = S, Se) и $Cs_2M(SO_4)_2{\cdot}6H_2O$ (M = Mg, Co, Ni, Z). It was determined that the metal sulphates and selenates have a strong salting impact on the solutions of rubidium and caesium sulphate and selenate.

B. 2. Characterization of developed Tuton salts by X-Ray powder diffraction

With the results of X-Ray powder diffraction and utilizing ITO and LSUCR codes the parameters of the following unit-cell cells were determined, among them:

$Rb_2M(SeO_4)_2{\cdot}6H_2O$ (M = Mg, Ni, Cu)
$Rb_2M(SO_4)_2{\cdot}6H_2O$ (M = Mg, Co, Ni, Cu, Zn)
$Cs_2M(SO_4)_2{\cdot}6H_2O$ (M = Mg, Co, Ni, Zn)

The values of the parameters of the unit-cell cells of the double salts $Rb_2M(XO_4)_2{\cdot}6H_2O$ (M = Mg, Co, Ni, Cu, Zn; X = S, Se) и $Cs_2M(SO_4)_2{\cdot}6H_2O$ (M = Mg, Co, Ni, Zn) are to close to the ones determined by X-Ray spectra of single-crystal.

B. 3. Infrared spectroscopic studies of double salts. Correlations between crystal structures and infrared spectra. Factor group analysis.

B. 3. 1. Analysis of normal vibrations of sulphate and selenate ions

The analyzed infrared spectra of the studies Tuton salts allow correlations between the vibration bands and their crystal structures to be done. Factor group analyzes demonstrating the relationship between the normal vibrations of the atomic groups SO_4^{2-} and SeO_4^{2-} ions, water molecules and their positional symmetries were developed.

The infrared spectra of the Tuton salts have a small number of infrared bands corresponding to asymmetric valence vibrations ν_3, less than the expected one, following the group analysis (C_1 positional symmetry of tetrahedron ions, i.e. six band should be expected).

The sulphate ions in the infrared spectra show three bands for ν_3, but the difference in the values of the wavenumbers of the low-frequency bands ($\Delta\nu$) is in the spectral interval of 10–12 cm^{-1}. The selenate ions in $Rb_2M(SeO_4)_2{\cdot}6H_2O$ (M = Mg, Co, Ni, Cu, Zn) and $Cs_2M(SeO_4)_2{\cdot}6H_2O$ (M = Mg, Co, Zn) are characterized with two bands of asymmetric vibrations ν_3, that is, these ions demonstrate a molecular symmetry which is greater than of the determined crystallographic one (effective spectroscopic symmetry C_{3v}).

The selenate ions in $Cs_2Ni(SeO_4)_2{\cdot}6H_2O$ show a molecular symmetry close to T_d (one infrared band for ν_3). The infrared bands corresponding to the symmetric valence vibrations ν_1 of the sulphate and selenate ions are of low intensities, which indicates low levels of energetic deformations, determined by structural data. The asymmetric vibrations ν_4 of sulphate and selenate ions are observed as doublets (630–610 cm^{-1} for the sulphate and 430–406 cm^{-1} for the selenate ions).

B. 3. 2. Assessments of the hydrogen bond strength in the investigated Tuton slats

Following the structural data bout the Tuton salts, there are three different crystallographic water molecules with positional symmetry C_1 and it follows that the appearance of six infrared bands in the high-frequency zone has to be expected, corresponding to ν_3 (asymmetric valence) and ν_1 (symmetric valence) of the water molecules. As a result of the strong interactions of identical oscillators O–H in the spectra there exists only one band. It was established that the water molecules in the selenate salts form stronger hydrogen bonds than in the case of sulphate salts due to the stronger proton accepting capacity of the selenate ions. Moreover, it was established that the strongest hydrogen bonds appear in the zinc salts due to the strong interaction of the relationship $Zn{-}OH_2$ (synergetic effect), while the weaker ones are formed in the magnesium salts as a result of the effect of the relationship $Mg{-}OH_2$.

The infrared spectra reveal a complex spectral picture in the area of vibrational deformations ν_2 of the water molecules (1730–1540 cm^{-1}) due to internal and intermolecular interactions ν_2, and overtones with/or combinational vibrations of water molecule librations.

Libration vibrations of water molecules are observed in the range of 1000 cm^{-1} and would be expected for band overlappings to appear, that correspond to the vibrational spectra of sulphate and selenate ions.

The water molecules of in the studied salts are characterized by two types of librations – rocking и wagging. The rocking vibrations are observed where the wavenumbers are high (in the range of 870–700 cm^{-1}) due to water molecules forming stronger hydrogen bonds because of shorter lengths of the connections $M{-}OH_2$. In the infrared spectra of the selenate salts, there are two distinct groups of librations. In the first group, the range is 750–710 cm^{-1} (rocking) while for the second one the range is 630–600 cm^{-1} (wagging); both ranges are free of vibrations of other atomic groups. The infrared spectra in the 580–510 cm^{-1} of the sulphate salts are strongly influenced by the deformation vibrations and the wavenumbers of the sulphate ions and in such cases, and they cannot be determined exactly.

B. 3. 3. Investigation of vibrational behavior of matrix-isolated SO_4^{2-} ions in selenate matrices and NH_4^+ ions in matrix-isolated sulphate and selenate matrices. Degrees of energetic deformations of matrix-isolated ions.

Natural resources and minerals as well as modern inorganic materials of high technologies are compounds with contents varying due to various contaminations by ions included in the structure of the main component (by replacement of ions in the matrix, when solids are at issue, or by the occupation of free crystallographic positions when solid solutions are considered). Inclusions of contaminating ions in solids lead to changes in the structural characteristics of the structure of the body in general, and this results in changes in the material properties.

In the last years, the matrix infrared spectroscopy has been successfully applied as a fast and reliable method for the determination of gest-ions and the nature of their inclusions, mechanical or by replacement (isomorphic, isodimorphic) or by intercalation. There are some versions of the matrix spectroscopy, and the versions are dependent on the type and number of matrix-isolated ions and molecules, such as a technique of the isotopic dissolution, solid-state spectroscopy, double-matrix spectroscopy, etc. Ions included in crystals of the host salt by isomorphic and isodimorphic replacement have spectra different from the spectra of the sal which the host salt forms with cations equal to the host. One principle advantage of the spectroscopic method is its sensibility concerning the concentrations of the included ions.

B. 3. 3. 1. Vibrational behavior of SO_4^{2-} ions included in crystals of $M'_2M''(SeO_4)_2{\cdot}6H_2O$ (M' = K, NH_4^+, Rb, Cs; M'' = Mg, Co, Ni, Zn).

Mixed crystals of $K_2M(SeO_4)_{2-x}(SO_4)_x{\cdot}6H_2O$, $(NH_4)_2M(SeO_4)_{2-x}(SO_4)_x{\cdot}6H_2O$, $Rb_2M(SeO_4)_{2-x}(SO_4)_x{\cdot}6H_2O$ и $Cs_2M(SeO_4)_{2-x}(SO_4)_x{\cdot}6H_2O$ (M = Mg, Co, Ni, Zn; x = 0.02, 0.10 и 0.15) have been synthesized and analysed by infrared spectra, in the are of valence vibration of matrix-isolated sulphate ions. A comparative analysis of the vibrational behavior of sulphate ions included in different selenate matrices - $M'_2M''(SeO_4)_{2-x}(SO_4)_x{\cdot}6H_2O$ (M' = K, NH_4^+, Rb, Cs; M'' = Mg, Co, Ni, Zn) have been carried out.

The degree of energetic deformations of the matrix-isolated sulphate ions was estimated using the values of $\Delta\nu_{as}$ (the difference in the frequencies of the components of the asymmetric valence and deformation vibrations), and $\Delta\nu_{max}$ (difference in the frequencies of high-frequency and low-frequency components of valence and deformation vibrations), as well by ratio $\Delta\nu_{as}/\nu_c$ (where **c** is the mean value of the wavenumbers of the asymmetric valence vibrations of sulphate ions).

It was established that the matrix-isolated SO_4^{2-} ions in selenate matrices (approximately 2 mol%) reveal three bands corresponding to ν_3, and one band corresponding to ν_1, by the low positional symmetry C_1 of the host selenate ions.

It was established that when the greater in size SeO_4^{2-} ions are replaced by smaller ce SO_4^{2-} ions, then the mean values of the asymmetric valence vibrations $\bar{\nu}_3$ of the sulphate ions are shifted towards lower wavenumbers, compared with the situation with the same ions in sulphate salts as a result of the lower repulsive potential of the selenate matrices, that is larger volumes of unit-cell cells of selenate salts.

It was established that the energetic deformation of the sulphate ions of Tuton sulphates, based on $\Delta\nu_3$ values, is stronger concerning the matrix-isolated sulphate ions, in selenate matrices, which is an indicator for a weak electrostatic field at the positions where the host ions are localized.

The values of $\Delta\nu_3$ and $\Delta\nu_3/\nu_c$ of the matrix-isolated sulphate ions increases in the following order: potassium, rubidium and caesium selenate matrices, due to larger volumes of the elementary cells of the caesium selenates and the respectively lower repulsive potential of these matrices.

It was established that the increase in the sulphate ion concentrations, included in the crystal of the selenate matrices, reduces the number of the infrared bands corresponding to ν_3.

B. 3. 3. 2. Vibrational behavior of NH_4^+ ions included in crystals $M'_2M''(XO_4)_2\cdot6H_2O$ (M' = K, Rb, Cs; M'' =Mg, Co, Ni, Zn; X = S, Se).

Mixed crystals of $M'_{2-x}(NH_4)_xM(XO_4)_2\cdot6H_2O$ (M′ = K, Rb, Cs; M″==Mg, Co, Ni, Zn; X = S, Se; x = 0.02, 0.05, 0.10, 0.15) have been developed and the vibrational *behavior* of the included NH_4^+ ions (in the area of asymmetric deformation vibrations ν_4, as the only vibrational zone of the ammonia ions which is free of vibrations related to other atomic groups. The research interest concerning such types of mixed crystals is mainly determined by the possibility to increase the permeability of the matrix by inclusions of ammonia ions.

The infrared spectra reveal that the isomorphic inclusions of ammonia ions in potassium, rubidium and caesium sulphate waters yield three bands corresponding to ν_4, which is related to the lower positional C_1 symmetry of hot ions of potassium, caesium and rubidium, respectively.

The isomorphic inclusion of ammonium in potassium, caesium and rubidium selenate matrices, however, results in the appearance of four bands related to ν_4 (except concerning the magnesium compound).

It was conceived a hypothesis that the appearance of more than expected infrared bands of ν_4, following the symmetry analysis, can be contributed to some extent, to existing disorder in the new structures as a result of formations of more than four hydrogen bonds. The difference in the vibrational behaviours of the ammonium ions in different matrices can be attributed to the stronger proton acceptor capacity of the selenate ions, i.e. the possibility of the oxygen atoms of the selenate ions linking to more than one proton.

B. 3. 4. Analysis of the releasing vibrations of water molecules in mixed crystals

The strength of the hydrogen bonds in the pure Tuton compounds, as well as in the corresponding potassium, rubidium and caesium compounds, containing isomorphic ammonium ions, is discussed using the wavenumbers of the water librations.

The infrared spectra reveal that the bands corresponding to the libration vibrations of the water molecules in the mixed crystals are increasing in width and shifted towards lower wavenumbers, and lower hydrogen bonds, respectively, because these bonds are weaker in mixed crystals in the case of pure potassium, rubidium and caesium salts. These spectroscopic results are due to a reduction in the proton acceptor capacities of sulphate (and selenate) ions in ammonium host ions (anti-cooperative or proton acceptor competitive effect). Moreover, the shift in the bands in the spectra of the selenate matrices is greater than the similar situation with the spectra of sulphate ions because in such cases the sulphates have a stronger proton acceptor capacity than the selenate ions.

The crystal structures of the synthesized single-crystal $M_2'Ni(XO_4)_2 \cdot 6H_2O$ (M' = Rb, Cs; X = S, Se) were decoded by X-ray diffraction. It was found relationships between the parameters of the unit-cell cells in the interatomic distances and the contents of the mixed crystals. The X-ray measurement of the crystal structures confirms the concept that the reduction of the hydrogen bond strengths, formed by water molecules is due to an increase in concentrations of the ammonium ions (there is an increase in the hydrogen bond lengths).

The disorder of the ammonium ions or the formation of bi and polyfurcate N–H···O–Se hydrogen bonds are not observed in the diffraction diagrams, but they can be avoided when the concentrations of the ammonium ions increase.

C. Synthesis and studies of bioactive substances (publications5A, 6B, 7B, 8B, 9B, 10B, 11A, 18A, 19A, 20A, 21A, 22A, 23A, 27C)

Bioactive substances affect the metabolic processes in the human body. A part of this effect is due to bonding with different enzymes playing key roles for the process. As a result, in some cases, there is a disbalance leading to different degree and type of diseases. A typical example is that increasing in the concentration of active radicals in the body leads to increase of undesired chemical transformations of bio-macromolecules. This, in turn, leads to difficulty in their functions and lowering of the body's defenses. Such changes force processes of physiological transformations in the body related to ageing and the appearance of cancers, cardiac problems, neurodegenerative diseases, etc. One of the most frequently encountered performances of such body dysfunction in the field of neurodegenerative problems is Alzheimer's disease (AD) and multiple sclerosis. They are related to abnormal changes in various parts of the human body. Some investigations reveal that during AD the process of aggregation of shortened peptide fragments in senile plaques and neurofibrillar tangles of the human brain leads to the bonding of the microelements normally presented in the brain such as Al, Fe, Cu, Zn. The brain activity depends on the optimal concentrations of some metals and many mechanisms control their concentrations, transport and releasing. The increase in the concentrations of the metals mentioned above yields impairments and metabolic dysfunctions in regulations of many proteins. The brain has effective homeostatic mechanisms and buffers for protection against unusual changes in the amounts of the metal ions. Abnormal metal-protein interactions *in vivo* are most likely due to altered copper, zinc, and iron metabolism in the brain. It turns out that a large number of biologically active substances have the ability to form complexes with metal ions, thus being used as transporter systems to introduce these ions into various parts of the human body. In addition, often the formed complexes have better hydrolytic stability at the pH of the human organism, as well as improved pharmacodynamic and pharmacokinetic properties, among which they contribute to the better bioavailability of the target carrier molecule. All this has caused in recent years a huge interest in researching the possibilities of inhibiting the precipitation process of these metals, which are key to the normal functioning of the brain.

An important group of biologically active substances with confirmed antioxidant features are polyphenolic compounds, i.e. the so-called flavonoids. They are natural substances whose activities are due to the ability to react with oxygen radicals and to form stable complexes with metallic ions, which are the main reasons for generating new radicals in the human body. The investigations of the biochemical reasons resulting in human body dysfunctions caused by active radicals are among the most challenging problems in contemporary science.

C. 1. Synthesis and studies of peptide-based

Organic ligands have been synthesized with the main task to choose antiaggregant peptides oriented to treatments of patients with Alzheimer's disease. The synthesized ligands include anti-aggregative motive related to Galanthamine, commonly used in the treatment of this disease, as a second pharmacophore.

The first series of ligands include anti-aggregative peptide Leu-Pro-Tyr-Phe-Asp at a position 6 and of 11 [11-N-Demethyl-N-[Boc-Leu-Pro-Tyr-Phe-Asp(OBzl)]-Galanthamine, studied by incremental connection to Boc-Asp(OBzl)-OH, Boc-Phe-OH, Boc-Tyr-OH, Boc-Pro-OH, Boc-Leu-OH към N-demethyllgalanthamine (norgalanthmime). The condensing agent chosen was TBTU/DIPEA. The second peptide 6-O-[Boc-Leu-Pro-Tyr-Phe-Asp(OBzl)-Gal]-Galanthamin was obtained by incremental connection to Boc-Asp(OBzl)-OH, Boc-Phe-OH, Boc-Tyr-OH, Boc-Pro-OH, Boc-Leu-OH to H-Gly-OGal, where with the latter the same condensation method was applied.

The compounds obtained own the desired combined activities concerning the inhibition of β-amyloid aggregation and inhibition of acetylcholinesterase. Thes compounds are planned as precursors for the synthesis of substances including glycoside residuals.

Cardiovascular diseases such as ischemic disease of the heart, microcard infarct, insult, etc. are leading reasons for lethal ends. The main reasons are the undesired coagulations and aggregations of blood platelets. Because of that, the search for new chemical substances affecting platelet aggregation is one of the principal tasks in medical practice. In the context of the results of the applicant, this task has two directions with scientific contributions, briefly outlined as follows:

1. An important contribution, in the context of the first direction, is the synthesis of new peptide-galanthamine derivatives including glycoside residuals. The design of these derivatives focuses on combinations of two anti-aggregative fragments peptide residuals and the galanthamine molecule. Glycoside residual is added to the obtained hybrid structure, thus adding a large number of OH groups allowing to obtain a good complex formation with various metals.These structures focus on the possibility to hold (capturing) metals such as Al, Zn, Fe and Cu and maintain their concentrations in normal ranges, thus controlling the formation of senile plaques during the development of Alzheimer's disease. The target product was obtained by the interaction of D-glucose and 6-O-[H-Leu-Val-Phe-Phe-Gly]-Galanthamine in presence of pyridine and acetic acid.

2. Triple peptide consequence Arg-Gly-Asp (RGD) is a peptide motive widely explored in many studies due to its well-known anti-aggregative, anti-cancer activities. In this context, the second contribution is related to the synthesis and studies of the anti-aggregative activity of new peptides RGD. These peptides resemble the γ/G-fragments (400-411) of the human fibrinogen

by including an active consequence RGD (Arg-Gly-Asp). It was discovered that the most active is the peptide Ala-Arg-Gly-Asp-Val, with a moderate size. Concerning the activity obtained of this peptide, the *in vitro* anti-platelet aggregation of water extracts of plants containing tannins was studied. It was proved that four such extracts can inhibit the platelet aggregation of about 55 and 90%. Two of the compounds have very high anti-aggregative effects.

- The formation of senile plaques and neurofibrillary knots in patients with Alzheimer's disease is a function of disruption of the β-amyloid precursor protein due to the action of enzymes named α-, β- и γ-secretases. In the course of the studies carried out new derivatives of the galantamine containing glycoside, and residuals were developed and their inhibiting activity concerning the activity of the β-secretase and anti-aggregative potential were studied. All new derivatives of the galanthamine containing modifications of tetrapeptide Leu-Val-Phe-Phe (Aβ17-Aβ20) were synthesized in a solution through fragments of consequent condensation methods. The compounds were tested *in vitro* for β-secretase inhibition activities utilizing the fluorescent method. All results reveal suppressing the β-secretase activities. Two of the new compounds have high activity while three of them exhibit moderate activities.

The studies on the structural activity reveal that the most successful are the modifications of the peptide chain containing norvaline or tertiary leucine, instead valine in Aβ17-Aβ20 or a free amino group in the N-end. The *in vitro* study concerning the anti-aggregative activity on plasma rich of platelet of sheep reveals that four of the tested compounds can inhibit platelet aggregation. Two of them, 6-O[H-Leu-Val-Phe-Phe-Gly]Gal and 6-O[H-Leu-Tle-Phe-Phe-Gly]Gal, containing 17-20 Aβ, including tertiary Leu instead Val in the molecule, have strong anti-aggregative effect when the level of IC_{50} is low.

- The anty cancer treatments are old and permanent tasks with intensive studies. At this moment the hybrid molecules are promising alternatives to the standard chemical therapies for cancer treatment. In this direction, new bio-conjugates analogues of BIM-23052 containing the second pharmacophore such as naphthalimide, caffeic acid, or three-peptide Arg-Gly-Asp, were developed.

The biological evaluation and the mathematical calculations of docking and hydrolytic stability were tested. all new molecules are obtained by a standard peptide synthesis on a solid polymer substrate. The anti-cancer potential was studied on a panel with cancer cell lines including human carcinoma of mammary gland MCF-7 (ER+, PR+ and Her-2-); MDA-MB-231 (ER-, PR- and Her-2-), as well as cell lines BALB 3T3 (mouse embryos fibroblasts) and MCF-10A (human epithelium cell line breast). The values of IC_{50}, for the cell line за MCF-10A were evaluated and used to calculate the selective index (SI). The highest selective index concerning MCF-7 is about 2,62 is related to the compound Npht-Gly-D-Phe-Phe(4-F)-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2. In the cells MCF-10 the weaker antiproliferative effect was due to the same compound (IC_{50} = 622,9 ± 23,91 μM), which indicates that this is a potential candidate for anti-cancer treatment. The studies on the hydrolytic stability reveal that is the most its lower anti-cancer activity and selectivity compared to Npht-Gly-D-Phe-Phe(4-F)-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2, the compound Arg-Gly-Asp-D-Phe-Phe(4-F)-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2 is the best candidate among the three bio conjugates for practical applications due to the synergetic effects fo activity profiles and stability. The mathematical docking calculations indicate that the synthesized bioconjugates show selectivities concerning various somatostatin receptors at the surfaces of various cell lines.

- These are good candidates as anti-cancer agents since they exist in the human body and the missing secondary effects of peptides. One representative of this peptide group with anti-microbial properties and good anti-cancer activity (KLAKLAK)$_2$. The derivation of target molecules and analogues of (KLAKLAK)$_2$-NH$_2$ was carried out by a solid-state peptide synthesis (Fmoc-strategy). The purities of all substances were tested by HPLC, while the structures were confirmed by mass spectroscopies. The cytotoxicity and the antiproliferative effects were studied utilizing 3T3 NRU and MTT tests. The method of disc diffusion was used to study the anti-microbial activity. The hydrolytic stability at three different, imitating the physiological pH of the body, was tested by HPLC.

The conjugates NphtG-(KLAKLAK)$_2$-NH$_2$ and Caf-(KLAKLAK)$_2$-NH$_2$ reveal good selective indices MCF-7 cancer cell lines, in addition to good cytotoxicity and antiproliferative effects. These compounds demonstrated good anti-mycotic activities and complete hydrolytic stability over 72 hours. The compound Caf-(KLβ-AKLβ-AK)$_2$-NH$_2$, containing β-Ala in its structures reveals good anti-microbial activity against *Escherichia coli* K12 407 and *Bacillus subtilis* 3562, in a combination with good antiproliferative effects and hydrolytic stability. The results obtained reveal that all synthesized conjugates can be successfully applied in the medical practice as anti-cancer and anti-mycotic agents

- It is well-known that the addition of various peptides to semen subjected to cryogenic conservation results in protective effects allowing its consequent applications. In this context, the effect of ultra-low temperatures of cryogenic conservation technology on the activity of enzymes lactate dehydrogenase and gamma-glutaminetransferase in the ejaculates of Ovis animals. The enzymatic activity of the spermatozoids in intracellular and plasma (external cellular activity before and after ejaculate thawing was studied. It was obtained, that after cryogenic conservation, the extracellular activity of the enzymes lactate dehydrogenase and the intracellular activities of the enzymes are reduced. The behaviour was observed with the enzyme gamma-glutaminetransferase. At ultra-low temperatures, the cryogenic conservations reduce the activity of lactate dehydrogenase and gamma-glutaminetransferase in the ejaculates of animals of type Ovis.

C.2. Synthesis and studies of phenolic compounds

- Hydroxuflavonic chelates iron and copper ions and in this way prevent formations of new active radicals in experiments performed *in vivo*. Moreover, in the contemporary literary sources, there is no common opinion about the chemical mechanisms forming such compounds, very important for the human life

In this context, 3-hydroxiflavone complexes with copper ions were synthesized, upon various pH and different ratios of metal./ligand and their DPPH activities were studied.

The structures of the developed complexes was confirmed by spectral metrhods and elemental analyzes. Quantum-chemical studies with DFT on their structures were carried out. These complexes were tested with DPPH for activities. The results reveal that these complexes exhibit to a greater extent pro-oxidant rather than anti-oxidant activities, and this performance reduces with a decrease in the relative amount of metal ions in them.

- By means of semi-empirical quantum–chemical method (AM1) and molecular mechanics, utilizing the code Hyprchem 8.0 Professional edition, an optimal series of Galacthamine containing peptides, with good inhibiting activities concerning AcChE and

ButChE was developped. First, it was carried aout a conformal search for all torsional angles at the molecular level mechanics. The generated about 10 000 geometries for each peptide allowed to select only four with the lowest energies. These four space structures were again optimised at the quantum-chemical level. The geometry obtained was lowest energy was used to calculate two descriptors related to the ability to ligand-receptor actions such as polarization, log P and energy of hydration. The calculated descriptors of peptides, not synthesized yet, are compared to the ones already synthesized and tested as inhibitors, especially those that demonstrate high inhibitions concerning ButChE.

The descriptor values are polarization between 500 and 515 au, hydration energy between –16 –17 kcal/mol and log P –3.53.

The closest lipophilicity to the leading peptides belongs to only five peptides. The other ones are too hydrophilic and therefore not suitable for synthesis (log P >3.23).

Sevent peptides have polarizabilities close to the leading ones. The others are too polarizable.

All compounds studied have hydration energies greater than the hydration energies of the leading peptides (18 kcal/mol).

If we assume that the higher polarizabilities are not the desirable polar and compare the lipophilicities of the studied compounds, then it follows that:

- Peptide(11-N-Demethyl-11-NN-[nicotinoyl-Asp(Asp-Leu-Ala-Val-NHBzl)]-Galanthamine) and
- Peptide 20 (11-N-Demethyl-11-N-N-[Iso-nicotinoyl-Asp(Asp-Leu-Ala-ValNH-Bzl)]-Galanthamine) are the most suitable for synthesis.

The calculations of the thermodynamic functions of the transitional compounds of a given reaction provide information about the reactivity of the reactants and the reaction mechanism, following the Hammond principle.

A series of 3-phenylcoumarins, already synthesized have been studied. These compounds have radical-capturing activities and their activity has been assessed. The calculated enthalpies of dissociations of the на O-H bonds have been evaluated by three different mechanisms. The roles of the positions of the hydroxyl group and the effects of the other groups on its reactivity. These enthalpies are good descriptors for the ability of the compound studied to react, determined experimentally. Moreover, the enthalpies of disassociation are possible to indicate the most probable reaction pathway concerning the active radicals.

The geometry of each of these 3- phenylcoumarins was optimized by the B3LYP/DFT фунfunctional and the standard 6-311++G(d,p) orbital basis. The calculations were performed by the implicit account of the effect of the dissolvent by the PCM/SCRF method. All quantum chemical studies were carried out by the code Gaussia’16.

Hydroxycoumarins are compounds with antioxidant properties and may serve as medicines. Moreover, they are isomers of the coumarins. Another important class are the plant metabolites.

As a result of the study, the following points may be outlined:

(1) The existence of the carboxyl group in these compounds hinders their planarities, that to some extent, might allow an extension of the coupled system and increase the effects of the functional groups in the coumarin and phenyl fragments of the molecule.

(2) Taking into account the polarizing action of the solvent (water) ETEs of the compounds studied are about 69–120 kJ/mol, which are lower than their BDEs, and BDEs are lower than IP

with about 11–50 kJ/mol. Therefore, the most possible mechanism of interaction between 3-phenylcoumarins and the free radicals is SPLET.

(3) Comparing the unmeasurable experimentally radical capturing activities and the calculated by ETE, it follows that there is an almost linear correlation. This direct supports that SPLET mechanism of capturing radicals is the main reaction mechanism.

C. 3. Application of the method of structural analysis for studies of bioactive substances and materials.

The combinations of methods and analyzes allow us to elucidate to a greater extent the properties of the studied object and increases the result's reliability. Nowadays, bioanalytical techniques, including liquid and gas chromatographies, combined with various sensors are widely encountered in scientific practice.

The type of the sensor (detector) depends on the threshold as well as on the matrix, where the target compounds have to be determined. In this context, results obtained in the last decade, related to the determination of six illegal substances such as sildenafil, tadalafil, vardenafil, dapoxetine, yohimbine and sibutramine, as well as their derivatives in food additives have been determined by high-efficiency liquid chromatography combined with mass spectroscopy or UV detection. All these compounds are of great interest because they are frequently used in food additives distributed via online markets.

Determination of the reaction speeds, mechanism and dynamics, including also reactions between organic and inorganic substances, biotransformations with enzyme participation, catalytic processes, etc., are of key importance in the determination of suitable technologies in various industries.

The transformation of the substrate from the raw resources towards end products, in some cases, is dependent on the reaction rates or specific conditions such as pressure, and temperature of catalytic activity. Because of this, the correct information about the proper reaction mechanism and the reaction dynamics is of primary importance considering maximal yields and purities of the desired products. Moreover, it is important to ensure complete reaction performance with minimal loss of time because all these factors directly affect the cost efficiency of the end product.

Applying infrared spectroscopy it is possible to control the dynamics of model reactions of acetylation of transformations of p-aminophenol towards paracetamol. The main reaction was monitored utilizing a preliminary selection of solvents, suitable to the requirements of the technique used paracetamol and the proper IR bands characterizing the transformation process.

Possibilities to apply cementations onto natural magnetite to recover silver from spent photographic solutions were investigated. The effects of the amount of the solid phase, preliminary treatment with sulphuric acid and the starting PH of the solutions on the amount of recovered silver have been studied. Some ad hoc experiments on preliminary treatments of the solution with selenic and telluric acids have been also performed.

A non-Arrhenius model based on the Mittag-Leffler function has been conceived as a basic concept. This approach allows modelling both sub-Arrhenius and super-Arrhenius behaviours and giving rise to modified temperature integrals.

- Dielectric properties (dc and ac conductivities of monocrystals $Be(IO_3)_2{\cdot}4H_2O$ have been studied. Energies of activations along the three main axes of the crystals based on the temperature-dependent DC conductivity have been estimated.

The results are outcomes of joint work with a team from the UCTM, Institute of General and Inorganic Chemistry - BAS, Institute of Mineralogy and Crystallography at the University of Vienna, South-West University "Neofit Rilski" - Blagoevgrad, Medical Faculty of the Thracian University- Stara Zagora, Institute of Neurobiology-BAS

Their help and activities are highly appreciated!

PERESPECTIVES OF FUTURE WORKS

1. Development of complexes with Fe, Al, Cu и Zn of peptide-Galanthamine molecules considering the better performance in pharmacokinetics and pharmacodynamics and estimation of the effects of the metal ions on the bioactivities. Applications of modern spectral methods for characterization of the developed complexes.
2. Development of complexes of biogenic elements with organic peptide ligands considering the better performance in pharmacokinetics and pharmacodynamics and estimation of the effects of the metal ions on the bioactivities and search for synergetic effects.
3. Design, synthesis and investigation of radical capturing activities of compleses of phenolic compounds.
4. Investigations on the energy of stabilization in the crystal field of M^{2+} ions included in $M^{+}_{2}Mg^{2+}_{(1-x)}M^{2+}_{x}(SeO_4)_2 \cdot 6H_2O$ (M^{+} = K, NH_4, Rb, Cs; M^{2+} = Mn, Co, Ni, Cu, Zn).

Publication 1A

V. Karadjova, D. Kovacheva, D. Stoilova
"Double beryllium iodate dihydrates, $M_2Be(IO_3)_4 \cdot 2H_2O$ (M = K, NH_4^+, Rb): Preparation, X-ray powder diffraction and vibrational spectra"
Vibrational Spectroscopy, 68, 2013, 183-189.

The solubilities in the three-component systems $MeIO_3$–$Be(IO_3)_2$–H_2O (Me = K, NH_4^+, Rb, Cs) were studied at 25°C by the method of isothermal decrease of supersaturation. It has been established that double salts, $K_2Be(IO_3)_4 \cdot 2H_2O$, $(NH_4)_2Be(IO_3)_4 \cdot 2H_2O$ and $Rb_2Be(IO_3)_4 \cdot 2H_2O$, crystallize from the ternary solutions within wide concentration ranges. Both the X-ray powder diffraction and the spectroscopic studies (infrared and Raman) reveal that the title compounds are isostructural. They crystallize in the monoclinic space group $P2/m$ with lattice parameters: $K_2Be(IO_3)_4 \cdot 2H_2O$ - a = 14.218(5) Å, b = 6.747(2) Å, c = 5.765(2) Å, β = 98.74(4)°, V = 546.6(2) Å^3; $(NH_4)_2Be(IO_3)_4 \cdot 2H_2O$ - a = 14.414(4) Å, b = 6.838(2) Å, c = 5.947(2) Å, β = 99.52(4)°, V = 578.0(2) Å^3; $Rb_2Be(IO_3)_4 \cdot 2H_2O$ - a = 14.423(4) Å, b = 6.867(2) Å, c = 5.743(3) Å, β = 98.15(3)°, V = 562.9(3) Å^3.

Infrared spectroscopic experiments show that comparatively strong hydrogen bonds are formed in the potassium and rubidium salts as deduced from the wavenumbers of ν_{OD} of matrix-isolated HDO molecules (isotopically dilute samples) owing to the strong Be–OH_2 interactions (*synergetic* effect). However, the IO_3^- ions in the ammonium compound are involved in hydrogen bonds with NH_4^+ ions additionally to those with water molecules and as a result of these intermolecular interactions the proton acceptor strength of the iodate ions decreases (*anti*-cooperative effect), thus leading to the formation of weaker hydrogen bonds in this compound (bonds of moderate strength) as compared to those formed in the potassium and rubidium ones. The normal vibrations of other entities (IO_3^- ions and BeO_4 tetrahedra (skeleton vibrations)) are also discussed.

Keywords: Potassium beryllium iodate dihydrate; Ammonium beryllium iodate dihydrate; Rubidium beryllium iodate dihydrate; Solubility diagrams; X-ray powder diffraction; Vibrational spectra.

Publication 2B

V. Karadjova, M. Georgiev, D. Stoilova
„Preparation, X-ray powder diffraction and vibrational spectra of $(NH_4)_2Be(IO_3)_4{\cdot}2H_2O$ *and* $K_2Be(IO_3)_4{\cdot}2H_2O$*"*
Journal of Chemical Technology and Metallurgy, 47, 2012, 303-310.

The solubility in the three-component $MeIO_3$-$Be(IO_3)_2$-H_2O (Me = K, NH^+) systems at 25°C is studied by the method of isothermal decrease of supersaturation. It has been established that double salts, $K_2Be(IO_3)_4{\cdot}2H_2O$ and $(NH_4)_2Be(IO_3)_4{\cdot}2H_2O$, crystallized from the ternary solutions in wide concentration ranges. The X-ray powder diffraction as well as the vibration spectroscopic studies reveal that the title compounds are isostructural.

Comparatively strong hydrogen bonds are formed in the potassium compound analogically to other beryllium compounds owing to the strong Be-OH_2 interactions (*synergetic* effect) as deduced from the wavenumbers of ν_{OD} of matrix-isolated HDO molecules (isotopically dilute samples). The formation of weaker hydrogen bonds in the ammonium salt (bonds of moderate strength) than that in the potassium one is due to the decreasing proton acceptor capability of the IO_3^- ions. The latter are involved in hydrogen bonds with NH_4^+ ions additionally to those with water molecules and as a result of these molecular interactions the proton acceptor strength of the iodate ions decreases as compare to that of the same ions in the potassium compound (*anti*-cooperative effect). The normal vibrations of other entities (IO_3^- ions and BeO_4 tetrahedra (skeleton vibrations)) are also discussed. A hypothesis is made that probably at least two crystallographically different iodate ions exist in the structures. The water librations couple intensively with both the translatory modes of the BeO_4 tetrahedra and the normal modes of the iodate ions, thus resulting in small values of isotopic ratios $\nu_R(H_2O)/\nu_R(D_2O)$ (close to 1).

Keywords: potassium beryllium iodate dihydrate, ammonium beryllium iodate dihydrate, solubility diagrams, vibrational spectroscopy, hydrogen bond strength.

Publication 3B

V. Karadjova

“Crystallization in the three-component systems $Rb_2SeO_4–MeSeO_4–H_2O$ *(Me = Mg, Ni, Cu) at 25 °C”*

Journal of Chemical Technology and Metallurgy, 48, 2013, 316-325.

The solubility in the three-component systems $Rb_2SeO_4–MeSeO_4–H_2O$ (Me = Mg, Ni, Cu) is studied at 25°C by the method of isothermal decrease of supersaturation. It has been established that double compounds, $Rb_2Me(SeO_4)_2·6H_2O$ (Me = Mg, Ni, Cu), crystallize from the ternary solutions within wide concentration ranges. The X-ray diffraction data reveal that the title compounds crystallize in the monoclinic space group $P2_1/c$ (C_{2h}^5) with lattice parameters: $Rb_2Mg(SeO_4)_2·6H_2O$ – a = 6.353(3) Å, b = 12.674(5) Å, c = 9.412(3) Å, β = 105.22(2)° , V = 731.2(3) Å^3; $Rb_2Ni(SeO_4)_2·6H_2O$ – a = 6.349(1) Å, b = 12.617(2) Å, c = 9.324(2) Å, β = 105.35(1)°, V = 720.3(1) Å^3; $Rb_2Cu(SeO_4)_2·6H_2O$ – a = 6.361(1) Å, b = 12.569(2) Å, c = 9.414(2) Å, β = 104.68(1), V = 728.1(2) Å^3. The infrared spectra are discussed with respect to the normal vibrations of the selenate ions and water molecules. The unit-cell group theoretical treatment of the double salts is presented. Infrared spectroscopy experiments show that the *effective* spectroscopic symmetry of the selenate ions is close to C_{3v}. Comparatively strong hydrogen bonds are formed in the rubidium Tutton selenates as deduced from both the wavenumbers of the stretching modes of the water molecules and the water librations due to the strong proton acceptor strength of the selenate ions.

Keywords: Rubidium magnesium selenate hexahydrate, rubidium nickel selenate hexahydrate, rubidium copper selenate hexahydrate, solubility diagrams, X-ray powder diffraction, infrared spectra.

Publication 4B

V. Karadjova (Review),
"A correlation between structural and vibrational spectroscopic data of some beryllium sulfates and selenates"
Journal of Chemical Technology and Metallurgy, 51, 1, 2016, 5-31.

The present paper summarizes experimental results on the study of some beryllium compounds and is a part of a dissertation entitled "Synthesis, structure and properties of some beryllium salts – sulfates and selenates".
The solubility diagrams of the three-component systems $BeSeO_4{-}K_2SeO_4{-}H_2O$, $BeSO_4{-}Rb_2SO_4{-}H_2O$ and $BeSeO_4{-}MSeO_4{-}H_2O$ (M = Co, Ni, Cu, Zn) at 25 ºC are presented and the crystallization field widths of the solid phases are determined. The experimental results are discussed with respect to the complex formation processes in the ternary solutions and the solubility of the salt components in their binary solutions. New compounds, $Rb_2Be(SO_4)_2{\cdot}2H_2O$ and $K_2Be(SeO_4)_2{\cdot}2H_2O$, have been obtained as a result of the co-crystallization processes in the above systems.
Crystal structures of $BeSeO_4{\cdot}4H_2O$, $M_2Be(SO_4)_2{\cdot}2H_2O$ (M = K, Rb), and $K_2Be(SeO_4)_2{\cdot}2H_2O$ are determined from single crystal X-ray diffraction data. It has been established that the beryllium selenatetetrahydrate crystallizes in the orthorhombic space group *Cmca*. The X-ray diffraction measurements reveal that the double beryllium compounds are isostructural and crystallize in the monoclinic space group $P2_1/c$.
Vibrational spectra (infrared and Raman) are presented in the regions of the normal vibrations of the different motives building up the structures of the studied beryllium compounds. The vibrational spectra are discussed in the light of both the crystal structures of the beryllium salts and the crystal chemical properties of the different entities.
A special attention is paid on the influence of different crystal chemical factors on the strength of the hydrogen bonds formed in the beryllium compounds: Be−O interactions (*synergetic* effect); proton acceptor capacity of the selenate and sulfate ions; proton acceptor capacity of the different oxygen atoms calculated according to the Brown's bond valence theory; compositions of the beryllium tetrahedra (acidity of the water molecules); *anti*-cooperative effect (proton donor and proton acceptor competitive effect); repulsion potential of the lattice sites where the water molecules are located; sizes of M^+ cations. The intramolecular O−H bond distances are derived from the ν_{OD} vs. r_{OD} correlation curve [H.D. Lutz, C. Jung, J. Mol. Struct., 404, 1997, 63-66]. Water librations of protiated and deuterated samples are also discussed.
Crystal matrix infrared spectroscopy was applied to analyze: (i) The distribution of the SO_4^{2-} ions included in the structure of $K_2Be(SeO_4)_2{\cdot}2H_2O$ over the two crystallographically different positions. (ii)The molecular symmetry of the SeO_4^{2-} ions in $BeSeO_4{\cdot}4H_2O$ (matrix-isolated SO_4^{2-} guest ions). (iii) The strength of the hydrogen bonds (method of isotopic dilution; matrix-isolated HDO molecules).

***Keywords*:** Beryllium sulfates and selenates, Crystal structures, Vibrational spectroscopy, Hydrogen bond strength, Crystal matrix infrared spectroscopy.

Publication 5A

Zh. Velkov, D. Tsekova, **V. Karadjova,** L. Vezenkov
"Molecular modeling of galanthamine derivatives comprising peptide moiety: methods, targets and accuracy of results"
Bulgarian Chemical Communications 3, vol. 50, 2018, 452-458.

Using parametrical and semi-empirical quantum-chemical methods, three important descriptors of a series of peptides, linked to the molecule of galanthamine, were calculated. Studied compounds are planned as drugs for the prevention and treatment of Alzheimer's disease. The descriptors: polarizability, hydration energy and log P, undoubtedly have a bearing on the ability of the compounds to form strong enzyme-inhibitory complexes. Optimal geometries of the investigated peptides, as well as the intramolecular hydrogen bonds that define their structure were found. The most reliable structures defined on the basis of calculated descriptors are suggested.

Keywords: Alzheimer's disease, Galanthamine, Nicotinic acid, Isonicotinic acid, Cholinesterase inhibitor

Publication 6B

Lyubomir Vezenkov, Hasan Cena, Dancho Danalev, **Veronika Karadjova**, Daniela Tsekova, Ventzislav Bardarov, Nikolay Vassilev
"*New derivatives of galanthamine containing peptide fragment*"
Journal of Chemical Technology and Metallurgy, 55, 2, 2020, 251-260

New derivatives of galanthamine containing a peptide fragment with an antiaggregation activity are synthesized. Herein the process of synthesis, purification and characterization of the newly obtained compounds is described. Syntheses were performed by consecutive attachment of Boc-protected amino acids to either norgalanthamine or H-Gly-Ogal using TBTU/DIPEA and TCTU/DIPEA methods. The purification of final products was realized by treating with EtOAc or by HPLC. The newly compounds were characterized by TLC, NMR, m.p. and MS. Two pharmacological effects are expected to be combined in a single molecule: the anticholinesterase and the antiaggregation ones.

Keywords: Alzheimer’s disease, Acetylcholinesterase, Galanthamine, Norgalanthamine, Antiaggregation activity.

Publication 7B

Zdravka Zaharieva, Tsvetelina Foteva, **Veronika Karadjova**, Dancho Danalev,
"Determination of some prohibited substances in food supplements using HPLC with MS or UV detection – view on current development",
Journal of Chemical Technology and Metallurgy, 56, 6, 2021, 1141-1155.

Nowadays bioanalytical techniques including liquid and gas chromatography combined with different types of detectors are largely introduced in a practice. They are largely used for detection and control of substances and for monitoring of the whole production process. The type of detector depends on necessary levels of detection, but also on the matrix where aimed compounds have to be determined.

Herein are summarized data from the last ten years related to determination of six main prohibited substances sildenafil, tadalafil, vardenafil, dapoxetine, yohimbine and sibutramine as well as their derivatives in food supplements using high performance liquid chromatography combined with mass spectrometric or UV detection. All these compounds are in a large interest because they are introduced often in products freely distributed in the internet market.

Keywords: Sildenafil, Tadalafil, Vardenafil, Dapoxetine, Yohimbine, Sibutramine, HPLC/MS, HPLC/UV.

Publication 8B

Atanas Atanasov, **Veronika Karadjova**, Albena Andonova, Daniela Tsekova, Valentin Lozanov, Boryana Parashkevova, Ivan Mindov, Roumiana Todorova, Lyubomir Vezenkov
"Synthesis, isolation and biological activity studies of galanthamine derivatives including peptide moiety and tannins from medicinal pants",
Journal of Chemical Technology and Metallurgy, 57 (1), 2022, 32-38.

The search of a new chemical substances influencing platelet aggregation is a very important endeavor for medical practice. Among the compounds that have antiaggregating activity are some peptides, tannins, etc. Here we present antiaggregation activity of Arg-Gly-Asp (RGD) peptide derivatives. Synthetic procedures of new peptide-galantamine derivatives including also glucose moiety designed to possess such activity are included. The in vitro effect of water extract from 20 tannins-containing plants from Bulgarian flora on aggregation of modified rat platelet-rich plasma was investigated and seven of them (Corylus avellana L, Cydonia oblonga Mill, Dryopteris filix-mas (L.) Schott, Ephedra distachya L., Geum urbanum L., Primula officinalis (L.) Hill and Punica granatum L.) were able to inhibit platelet aggregation.

Keywords: RGD-peptides, Galanthamine, Medicinal plants, Tannin, Platelet aggregation, Rat.

Publication 9B

Maria Vakarelska-Popovska, **Veronika Karadjova**, Zhivko Velkov
"Synthesis, structure and prooxidant activity of 3-hydroxyflavone complexes with Cu(II)"
Journal of Chemical Technology and Metallurgy, 57 (3), 2022, 419-432.

Hydroxyflavones chelate iron and copper ions thus preventing the formation of new active radicals in experiments in vivo. Furthermore, it is reported that some of them demonstrate in vitro prooxidant activity in the presence of metal ions. Consequently, there is no unanimity in the literature on the chemical mechanisms that engender the properties of these compounds vital for the human health.

Herein, our investigations on the synthesis and DPPH activity of 3-hydroxyflavone complexes with copper ions obtained at different pH and different metal/ligand ratio are presented. Their structure was confirmed using spectral methods and elemental analyzes. A DFT quantum chemical study on the complexes structure was also performed. The resulting complexes were tested for activity against DPPH. The outcome show that the complexes exhibit prooxidant rather than antioxidant activity, which decreases with declining the relative metal ion content in the complexes.

***Keywords**:* Cu(II)/3-hydroxyflavone complexes, Synthesis, IR and UV spectra, DPPH-activity, quantum-chemical/ DFT investigation.

Publication 10B

Madlena Andreeva, **Veronika Karadjova**, Rossen Stefanov

"Investigation of the effect of ultra-low temperatures in cryopreservation on the activity of the enzymes lactate dehydrogenase and gamma-glutamyl transferase"

Journal of Chemical Technology and Metallurgy, 57 (2), 2022, 298-301.

The aim of the present study was to investigate the effect of ultra-low cryopreservation temperatures on the activity of the enzymes lactate dehydrogenase and gamma-glutamyl transferase in ejaculates of Ovis aries animals. For this purpose, 25 ejaculates from breeders of the species Ovis aries were examined. Cryopreservation of sperm was performed by the Cassou method (1964). Enzyme activity was determined in sperm cells (intracellular activity) and in sperm plasma (extracellular activity) before freezing and after thawing of ejaculates. After cryopreservation, the extracellular enzyme activity of lactate dehydrogenase decreased from 334.87 ± 20.54 U L^{-1} to 243.54 ± 21.85 U L^{-1}, and there was a decrease in the intracellular activity of the enzyme from 793.02 ± 36.74 U L^{-1} to 506.52 ± 44.46 U L^{-1}. Gamma-glutamyl transferase enzyme activity was also affected by cryopreservation. Its extracellular activity decreased from 58.84 ± 2.66 U L^{-1} to 38.52 ± 2.03 U L^{-1}, and its intracellular activity from 6.08 ± 0.27 U L^{-1} to 3.16 ± 0.14 U L^{-1}. In conclusion, ultra-low cryopreservation temperatures reduce the activity of lactate dehydrogenase and gamma-glutamyl transferase enzymes in the ejaculates of Ovis aries animals.

Keywords: Rams, Sperm, Cryopreservation, Lactate dehydrogenase, Gamma-glutamyl transferase

Publication 11A

M. Nadoliisky, M. Georgiev, D. Nikolova, **V. Karadjova**
“Dielectric properties of $Be(IO_3)_2{\cdot}4H_2O$ *crystals”*
Journal of Materials Science: Material2s in Electronics, 16, 2005, 667-678.

The article studies the dielectric properties, dc conductivity and ac conductivity of $Be(lO_3)_2.4H_2O$ single crystals. The dielectric constant e has been defined for the three directions of the vectors a, b and c in the crystals in the temperature interval 280-340 K and frequency range 100 Hz-106 Hz. The crystals show strongly expressed anisotropy, at 20°C and frequency 100 Hz $\varepsilon_a=235$, $\varepsilon_b=30$ and $\varepsilon_c=85$. The frequency dependence of e is evidence of the presence of low-frequency relaxation polarization in the crystals. The activation energies of the three directions in the crystals have been derived from the temperature dependence of dc conductivity, and they are 1.03 eV 0.836 eV and 1.2 eV respectively.

Publication 12B

V. Karadjova, M. Georgiev, D. Stoilova
“Solubility in the three-component systems $BeSeO_4$*–*$MeSeO_4$*–*H_2O *(Me = Co, Ni, Cu, Zn)”*
Journal of Chemical Technology and Metallurgy, 43, 2008, 418-423.

The three-component systems $BeSeO_4$–$MeSeO_4$–H_2O (Me = Co, Ni, Cu, Zn) have been studied by the method of physico-chemical analysis. Simple salts are formed in the title systems. The crystallization field widths are explained in terms of different solubility of the selenates in their binary solutions, respectively of different water activity.

Keywords: Solubility diagrams of the $BeSeO_4$–$MeSeO_4$–H_2O systems (Me = Co, Ni, Cu, Zn), Physico-chemical analysis, Crystallization field widths

Publication 13A

M. Wildner, **V. Karadjova**, D. Marinova, M. Georgiev, D. Stoilova
"Crystal and molecular structure of ammonium beryllium sulfate dihydrate $(NH_4)_2Be(SO_4)_2{\cdot}2H_2O$*"*
Journal of Molecular Structure, 1022, 2012, 117-124.

In this paper we report the crystal and molecular structure of the title compound, $(NH_4)_2Be(SO_4)_2{\cdot}2H_2O$, as determined by single-crystal X-ray diffraction and vibrational spectroscopy data. $(NH_4)_2Be(SO_4)_2{\cdot}2H_2O$ crystallizes in the monoclinic space group $P2_1/c$ (a = 11.448(2), b=11.876(2), c = 7.439(1) Å, b = 96.64(1)°, V = 1004.6 Å3, Z = 4, R1 = 0.036 for 3753 Fo > $4\sigma(F_o)$ and 185 variables), and is isotypic with the respective potassium and rubidium sulfates and the potassium selenate. The crystal structure is built from three-membered tetrahedral chain fragments, consisting of a central $BeO_2(H_2O)_2$ group and two adjacent SO_4 tetrahedra. These building blocks are linked by rather strong hydrogen bonds of the water molecules (O···O = 2.66–2.77 Å) and by moderate to weak hydrogen bonds of the NH_4 groups (N···O P 2.78 Å) to a three-dimensional framework structure. The infrared bands corresponding to the stretching modes ν_3 and ν_1 as well as the Raman band corresponding to ν_1 of the SO_4^{2-} ions are observed in the spectra as doublets, thus reflecting the existence of two crystallographically different sulfate ions. The spectroscopic experiments reveal that the sulfate tetrahedra exhibit a remarkably large extent of energetic distortion as deduced from the values of $\Delta\nu_3$ (site group splitting) and $\Delta\nu_{max}$ (the difference between the highest and the lowest wavenumbered component of the stretching modes) (111 and 183.5 cm^{-1}, respectively), which could not be predicted from the structural data. The comparison of the spectral region widths of the stretching and bending modes of the SO_4^{2-} ions allows us to assume that these ions undergo a stronger energetic distortion with respect to the SAO bond lengths than that with respect to the OASAO bond angles. The water librations couple intensively with both the translatory modes of the Be^{2+} cations (BeO_4 skeleton vibrations) and the normal modes of the sulfate ions, thus producing small isotopic shifts (for example, the ratio $\nu_r(H_2O)/\nu_r(D_2O)$ has value of 1.12). The strength of the hydrogen bonds formed by the water molecules in the title compound is also commented in comparison with that of the hydrogen bonds in the respective isomorphous potassium and rubidium compounds.

Keywords: Ammonium beryllium sulfate dehydrate; Crystal structure; Infrared and Raman spectroscopy; Distortion of the SO_4 tetrahedra; Water librations

Publication 14A

V. A. Karadjova, D. M. Marinova, M. P. Georgiev, D. Stoilova
„Ammonium beryllium selenate dihydrate, $(NH_4)_2Be(SeO_4)_2{\cdot}2H_2O$: Preparation, X-ray powder diffraction and vibrational spectra”
Vibrational Spectroscopy, 64, 2013, 39-43.

The solubility in the three-component $(NH_4)_2SeO_4$–$BeSeO_4$–H_2O system is studied at 25 °C by the method of isothermal decrease of supersaturation. $(NH_4)_2Be(SeO_4)_2{\cdot}2H_2O$ crystallizes from solutions containing 31.35 mass% beryllium selenate and 30.66 mass% ammonium selenate up to solutions containing 26.84 mass% beryllium selenate and 46.84 mass% ammonium selenate. The X-ray powder diffraction data show that $(NH_4)_2Be(SeO_4)_2{\cdot}2H_2O$ is isostructural with the respective $K_2Be(SeO_4)_2{\cdot}2H_2O$, $K_2Be(SO_4)_2{\cdot}2H_2O$ and $Rb_2Be(SO_4)_2{\cdot}2H_2O$. $(NH_4)_2Be(SeO_4)_2{\cdot}2H_2O$ crystallizes in the monoclinic space group $P2_1/c$: a = 11.747(3) Å, b = 12.212(4) Å, c = 7.649(2) Å, β = 96.94(3)°, V = 1089.3(3) Å^3, Z = 4. Vibrational spectra (infrared and Raman) of the title compound are presented and discussed with respect to the internal modes of both the ammonium and the selenate tetrahedra, hydrogen bond strengths and the lattice vibrations of the BeO_4 tetrahedra (skeleton vibrations).

Keywords: Ammonium beryllium selenate dihydrate; Thermal dehydration; X -ray powder diffraction, Vibrational spectra

Publication 15A

V. Karadjova, D. Stoilova
"Infrared spectroscopic study of $Rb_2M(XO_4)_2{\cdot}6H_2O$ *(Me = Mg, Co, Ni, Cu, Zn) and of* SO_4^{2-} *guest ions included in rubidium Tutton compounds",*
Journal of Molecular Structure, 1050, 2013, 204-210.

The solubility in the three-component systems Rb_2SeO_4–$MeSeO_4$–H_2O (Me = Mg, Ni, Cu) is studied at 25°C by the method of isothermal decrease of supersaturation. It has been established that double compounds, $Rb_2Me(SeO_4)_2{\cdot}6H_2O$ (Me = Mg, Ni, Cu), crystallize from the ternary solutions within wide concentration ranges.
Infrared spectra of rubidium Tutton compounds, $Rb_2Me(XO_4)_2{\cdot}6H_2O$ (X = S, Se; Me = Mg, Co, Ni, Cu, Zn) (in the region of 1300−400 cm^{-1}) as well as those of SO_4^{2-} ions included in selenate matrices (up to 15 mol%) in the region of the stretching modes ν_3 and ν_1 are presented and discussed. The matrix-isolated SO_4^{2-} ions exhibit three bands for ν_3 and one band for ν_1 in good agreement with the low site symmetry C_1 of the SeO_4^{2-} host ions. The extent of energetic distortion of the isomorphously included ions as deduced from the values of $\Delta\nu_3$ (site group splitting) and $\Delta\nu_3/\nu_c$ (where ν_c is the centro-frequency value of the asymmetric stretches) is discussed. The comparison of the vibrational behavior of the matrix-isolated SO_4^{2-} ions (about 2 mol%) in different Tutton selenate matrices show that the distortions of the sulfate guest ions increase on going from potassium selenates to ammonium ones. The stronger distortion of the SO_4^{2-} guest ions in ammonium compounds as compared to that of the same ions included in the potassium and rubidium selenates is due to the formation of hydrogen bonds between the guest ions and the NH_4^+ host cations additionally to those with water molecules of the host compound. The water librations are also briefly discussed.

***Keywords*:** Tutton compounds, $Rb_2Me(XO_4)_2{\cdot}6H_2O$ (Me = Mg, Co, Ni, Cu, Zn; X = S, Se); Solubility diagrams; Matrix-isolated SO_4^{2-} ions.

Publication 16A

V. Karadjova, D. Kovacheva, D. Stoilova
"Study on the cesium Tutton compounds, $Cs_2M(XO_4)_2·6H_2O$ (M = Mg, Co, Zn; X = S, Se): Preparation, X-ray powder diffraction and infrared spectra"
Vibrational Spectroscopy, 75, 2014, 51-58.

The crystallization processes in the three-component systems Cs_2SO_4–MSO_4–H_2O (M = Mg, Co, Zn) have been studied at 25°C. It has been established that cesium Tutton compounds, $Cs_2M(SO_4)_2·6H_2O$ (M = Mg, Co, Zn; X = S, Se), crystallize from the ternary solutions within large concentration ranges. The double salts were identified by means of X-ray powder diffraction and infrared spectroscopy. Infrared spectra of the cesium compounds are presented and discussed with respect to both the normal modes of the tetrahedral ions and the water molecules. The water librations are also discussed. The strength of the hydrogen bonds formed in the cesium salts as deduced from the frequencies of $ν_{OH}$ is commented. The analysis of the spectra reveals that stronger hydrogen bonds are formed in the cesium selenates as compared to those in the respective sulfates due to the stronger proton acceptor ability of the selenate ions.

Keywords: Cesium Tutton selenates and sulfates Solubility diagrams, Infrared spectra Strength of the hydrogen bonds, Energetic distortion of SO_4^{2-} and SeO_4^{2-} ions

Publication 17A

D. Manasieva, **V. Karadjova,** D. Stoilova

"Infrared spectroscopic study of SO_4^{2-} *ions included in* $Me_2^+Me^{2+}(SeO_4)_2\cdot 6H_2O$ *(*Me^+ *= K,* NH_4^+*;* Me^{2+} *= Mg, Co, Ni, Cu, Zn) and* NH_4^+ *ions included in* $K_2Me^{2+}(XO_4)_2\cdot 6H_2O$ *(X = S, Se;* Me^{2+} *= Mg, Co, Ni, Cu, Zn)"*

Spetrochmica Acta B, 134, 2015, 526-534.

Infrared spectra of Tutton compounds, $Me_2^+Me^{2+}(XO_4)_2\cdot 6H_2O$ (Me^+ = K, NH_4^+; Me^{2+} = Mg, Co, Ni, Cu, Zn; X = S, Se), as well as those of SO_4^{2-} guest ions included in selenate host lattices and of NH_4^+ guest ions included in potassium host lattices are presented and discussed in the regions of ν_3 and ν_1 of SO_4^{2-} guest ions, ν_4 of NH_4^+ guest ions and water librations.

The SO_4^{2-} guest ions matrix-isolated in selenate matrices (approximately 2 mol%) exhibit three bands corresponding to ν_3 and one band corresponding to ν_1 in good agreement with the low site symmetry C_1 of the host selenate ions. When the larger SeO_4^{2-} ions are replaced by the smaller SO_4^{2-} ions the mean values of the asymmetric stretching modes $\bar{\nu}_3$ of the included SO_4^{2-} ions are slightly shifted to lower frequencies as compared to those of the same ions in the neat sulfate compounds due to the smaller repulsion potential of the selenate matrices (larger unit-cell volumes of the selenates). It has been established that the extent of energetic distortion of the sulfate ions matrix-isolated in the ammonium selenates as deduced from the values of $\Delta\nu_3$ and $\Delta\nu_3/\nu_c$ is stronger than that of the same ions matrix-isolated in the potassium selenates due to the formation of hydrogen bonds between the SO_4^{2-} guest ions with both the water molecules in the host compounds and the NH_4^+ host ions (for example, $\Delta\nu_3$ of the sulfate guest ions have values of 30 and 51 cm^{-1} in the nickel potassium and ammonium compounds, and 33 and 49 cm^{-1} in the zinc potassium and ammonium compounds, respectively).

The infrared spectra of ammonium doped potassium sulfate matrices show three bands corresponding to ν_4 of the included ammonium ions in agreement with the low site symmetry C_1 of the host potassium ions. However, the inclusion of ammonium ions in selenate matrices (with exception of the magnesium compound) leads to the appearance of four bands in the region of ν_4. At that stage of our knowledge we assume that some kind of disorder of the ammonium ions included in selenate lattices occurs due to the different proton acceptor capability of the SO_4^{2-} and SeO_4^{2-} ions. The latter ions are known to exhibit stronger proton acceptor abilities. This fact will facilitate the formation of polyfurcate hydrogen bonds of the ammonium ions in the selenate matrices, thus leading to increasing in the coordination number of these ions, i.e. to a disorder of the ammonium guest ions.

The strengths of the hydrogen bonds formed in the title Tutton compounds as well as that of the hydrogen bonds in potassium compounds containing isomorphously included ammonium ions as deduced from the wavenumbers of the water librations are also discussed. The bands corresponding to water librations in the spectra of the mixed crystals $K_{1.8}(NH_4)_{0.2}Me(XO_4)_2\cdot 6H_2O$ (Me = Mg, Co, Ni, Cu, Zn; X = S, Se) broaden and shift to lower frequencies as compared to those of the potassium host compounds, thus indicating that weaker hydrogen bonds are formed in the mixed crystals. These spectroscopic findings are owing to the decrease in the proton acceptor capacity of the SO_4^{2-} and SeO_4^{2-} ions due to the formation of hydrogen bonds between the host anions and the guest ammonium cations additionally to water

molecules (*anti*-cooperative or proton acceptor competitive effect). Furthermore, the band shifts in the spectra of the selenate matrices are generally larger than those observed in the spectra of the respective sulfates due to the stronger proton acceptor ability of the selenate ions.

Keywords: Tutton compounds, $Me_2^{+}Me^{2+}(XO_4)_2\cdot 6H_2O$ (Me^{+} = K, NH_4^{+}, Me^{2+} = Mg, Co, Ni, Cu, Zn; X = S, Se), Crystal matrix infrared spectroscopy, Matrix-isolated SO_4^{2-} and NH_4^{+} guest ions, Energetic distortion of SO_4^{2-} guest ions, Water librations

Publication 18A

Jordan Hristov and **Veronika Karadjova,**
“On the p(x) approximation in the non-*isothermal reaction kinetics by a generalized exponential integral”*
Thermal Science, Vol. 25, Special Issue 2, 2021, S321-S326.

A non-Arrhenius model based on the Mittag-Leffler function has been conceived as a basic concept. This approach allows modelling both sub-Arrhenius and super- Arrhenius behaviours and giving rise to modified temperature integrals.

Keywords: non-Arrhenius, Mittag-Leffler function, Temperature integral

Publication 19A

Sirine Jaber, Veronica Nemska, Ivan Iliev, Elena Ivanova, Tsvetelina Foteva, Nelly Georgieva, Ivan Givechev, Emilia Naydenova, **Veronika Karadjova** and Dancho Danalev
“Synthesis and Biological Studies on (KLAKLAK)$_2$-NH$_2$ Analog Containing Unnatural Amino Acid β-Ala and Conjugates with Second Pharmacophore”
Molecules 26, 2021, 7321-7333.

Abstract: (1) Background: Peptides are good candidates for anticancer drugs due to their natural existence in the body and lack of secondary effects. (KLAKLAK)$_2$ is an antimicrobial peptide that also shows good anticancer properties.

(2) Methods: The Solid Phase Peptide Synthesis (Fmoc-strategy) was used for the synthesis of target molecules, analogs of (KLAKLAK)$_2$-NH$_2$. The purity of all compounds was monitored by HPLC, and their structures were proven using mass spectrometry. Cytotoxicity and antiproliferative effects were studied using 3T3 NRU and MTT tests, respectively. For determination of antimicrobial activity, the disc-diffusion method was used. Hydrolytic stability at three pH values, which mimic the physiological pH in the body, was investigated by means of the HPLC technique.

(3) Results: A good selective index against MCF-7 tumor cell lines, combined with good cytotoxicity and antiproliferative properties, was revealed for conjugates NphtG-(KLAKLAK)$_2$-NH$_2$ and Caf-(KLAKLAK)$_2$-NH$_2$. The same compounds showed very good antifungal properties and complete hydrolytic stability for 72 h. The compound Caf-(KLβ-AKLβ-AK)$_2$-NH$_2$ containing β-Ala in its structures exhibited good antimicrobial activity against *Escherichia coli* K12 407 and *Bacillus subtilis* 3562, in combination with very good antiproliferative and cytotoxic properties, as well as hydrolytic stability.

(4) Conclusions: The obtained results reveal that all synthesized conjugates could be useful for medical practice as anticancer or antimicrobial agents.

Keywords: (KLAKLAK)$_2$, Antitumor peptides, 1,8-naphthalimide, Caffeic acid, Unnatural amino acids

Publication 20A

Veronika Karadjova, Maria Vakarelska-Popovska, Zhivko Velkov
"Radical-scavenging activity characterization of a series of synthetic 3-phenylcoumarins"
Computational and Theoretical Chemistry, Vol. 1202, August 2021, 113300

A series of synthetic hydroxyl derivatives of 3-phenylcoumarin with already assessed radical-scavenging activity were modeled and treated with quantum-chemistry methods in order to get insight into the structural and energy changes occurring during dissociation of O–H bonds by different mechanisms. The enthalpy changes of each step were calculated and the role of the OH-group positions in the molecules, as well as the influence of the second hydroxyl group on the reactivity were evaluated. The geometry of each intermediate structure was optimized using B3LYP/DFT functional and the standard 6-311++G(d,p) orbital basis set. Solvent effects were accounted for using the SCRF method, via the polarized continuum method.

Keywords: 3-phenylcoumarins**,** Radical-scavenging activity**,** DFT-calculations**,** Mechanisms of O–H bond dissociations

Publication 21A

Lyubomir T. Vezenkov, Dancho L. Danalev, Iwan Iwanov, Valentin Lozanov, Atanas Atanasov,Rumyana Todorova, Nikolay G. Vassilev, Boyana Parvanova, **Veronika Karadjova**
"Synthesis and Biological Study of New galanthamine-peptide derivatives designed for prevention and treatment of Alzheimer's desease",
Amino Acids vol. 54, 2022, 897–910

The Alzheimer's disease leads to neurodegenerative processes and affecting negatively million people worldwide. The treatment of the disease is still difficult and incomplete in practice. Galanthamine is one of the most commonly used drugs against the illness. The main aim of this work is design and synthesis of new derivatives of galanthamine comprising peptide moiety as well as study of their β-secretase inhibitory activity and the anti-aggregating effect. All new derivatives of galanthamine containing analogues of Leu-Val-Phe-Phe (Aβ17-Aβ20) were synthesized in solution using fragment and consecutive condensation approaches. The new derivatives were characterized by melting points, NMR, and HPLC/MS. They were tested in vitro for β-secretase inhibition activity by means of fluorescent method and were investigated in vitro for anti-aggregation
activity on sheep platelet-rich plasma. Although the new compounds do not contain a structural element responsible for the β-secretase inhibition, five of them show high or good β-secretase inhibitory activity between 19.98 and 51.19% with IC_{50} between 1.95 and 5.26 nM. Four of the new molecules were able to inhibit platelet aggregation between 55.0 and 90.0% with IC_{50} between 0.69 and 1.36 μM. Four of the compounds were able to inhibit platelet aggregation and two of them have high anti-aggregating effects.

Keywords: Galanthamine; Alzheimer's disease; Amyloid peptide; Anti-aggregating peptide; β-Secretase inhibitors

Publication 22A

Dancho Danalev, Ivan Iliev, Dessislava Borisova, Tatyana Dzimbova, Tamara Pajpanova, Zdravka Zaharieva, **Veronika Karadjova**, Tsvetelina Foteva, Emilia Naydenova
"Synthesis, anticancer activity, docking calculations and hydrolytic stability studies of bioconjugates of monofluorenated analogue of BIM-23052",
Protein & Peptide Letters, vol. 29, issue 12, 2022.

*Background***:** The fight against cancer has started since its discovery and has not subsided to nowadays. Currently, the hybrid molecules have become a promising alternative to the standard chemotherapeutics for the treatment of multi-causal diseases, including cancers.
*Objective***:** Herein, we report the synthesis, biological evaluation, mathematical docking calculations and hydrolytic stability of the new bioconjugates of monofluorinated analogues of BIM-23052, containing second pharmacophore naphthalimide, caffeic acid or the tripeptide Arg-Gly-Asp.
*Methods***:** All new molecules are obtained using standard peptide synthesis on solid support. Anticancer potential is studied against a panel of tumor cell lines included human mammary carcinoma cell lines MCF-7 (ER+, PR+ and Her-2-); MDA-MB-231 (ER-, PR- and Her-2-), as well as cell lines BALB 3T3 (mouse embryonic fibroblasts) and MCF-10A (human breast epithelial cell line).
*Results***:** The IC50 values found in the MCF-10A cell line assay were used to calculate the selective
index (SI). The highest SI relative to MCF-7, with a value of 2.62 is shown by the compound Npht-
Gly-D-Phe-Phe(4-F)-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2. In MCF-10 cells, the weakest antiproliferative effect was caused by the same compound (IC_{50} = 622.9 ± 23.91 μM), which makes this analogue a good candidate for the new anticancer medical drug. Unfortunately, the hydrolytic stability studies reveal that this bioconjugate is the most unstable of hydrolysis under physiological
conditions in the body.
*Conclusion***:** Even with lower anticancer activity and selectivity in comparison with Npht-Gly-DPhe-Phe(4-F)-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2, the compound Arg-Gly-Asp-D-Phe-Phe(4-F)-Phe-D-Trp-Lys-Thr-Phe-Thr-NH2 is the best candidate between three investigated bioconjugates for practical application due to combination of activity and stability profiles. Mathematical docking calculation also reveals that synthesized bioconjugates show selectivity according to different
somatostatin receptors on the surface of different cell lines.

Keywords: Somatostatin analogues, BIM-23052, Anticancer activity, Docking simulation, Hydrolytic stability, Caffeic acid, 1,8-naphtalimide, RGD.

Publication 23B

Milena Nedkova-Shtipska, Sirine Jaber, Stoiko Petrin, **Veronika Karadjova**, Dancho Danalev
„Study of transformation of p-aminophenol in liquid phase with infrared spectroscopy“
Journal of Chemical Technology and Metallurgy, 57 (5), 2022.

Determining the rate, mechanism and dynamics of chemical reactions, including reactions between organic and inorganic substances, biotransformations involving enzymes, catalytic processes, etc. is key to setting the most appropriate technological parameters in various industries. The conversion of a substrate into a final product can go through various stages, some of which are speed-determining, while others require specific conditions - pressure, temperature, presence of catalyst and others. Therefore, clarifying the exact mechanism and dynamics of the transformation process is extremely important for achieving good yields and purity of the final products. It is also important to ensure the overall course of the transformation reaction, while minimizing the loss of time, as these factors directly affect the budget of the final product. The aim of the present study was to apply the features of IR spectroscopy to follow the dynamics of model acetylation reaction of transformations of p-aminophenol to paracetamol. Finally, we demonstrated the possibility IR spectroscopy in solution to be used as a technique for monitoring of specific transformation reaction in solution. The main reaction was successfully followed at time by preliminary selecting of the most suitable solvent, which is compatible with the requirements of the technique used and the monitored reaction as well as the right IR bands characteristic for the process of transformation.

Keywords: IR spectroscopy, Acetylation reaction, Paracetamol

Publication 24C

V. Karadjova, D. Stoilova

"Crystallization in the three-component systems Rb_2SO_4–MSO_4–H_2O (M = Mg, Co, Ni, Cu, Zn) at 298 K"

Journal of Crystallization Process and Technology 3, 2013, 136-147.

The crystallization in the three-component systems Rb_2SO_4–MSO_4–H_2O (M = Mg, Co, Ni, Cu, Zn) is studied by the method of isothermal decrease of supersaturation. It has been established that isostructural double compounds, $Rb_2M(SO_4)_2\cdot6H_2O$ (M = Mg, Co, Ni, Cu, Zn), (SG $P2_1/c$ (C_{2h}^5)), crystallize from the ternary solutions within wide concentration ranges. The infrared spectra are discussed with respect to the normal vibrations of the sulfate ions and water molecules. The unit-cell group theoretical treatment of the double salts is presented. The extent of energetic distortions of SO_4^{2-} guest ions (about 2 mol%) matrix-isolated in the respective selenates, $M_2'M''(SeO_4)_2\cdot6H_2O$ (M′ = K, Rb, NH_4^+; M″ = Mg, Co, Ni, Cu, Zn), is comented.

Keywords: $Rb_2Me(SO_4)_2\cdot6H_2O$ (Me = Mg, Co, Ni, Cu, Zn), Solubility Diagrams, X-Ray Powder Diffraction, Infrared Spectra, Matrix Infrared Spectroscopy

Publication 25C

V. Karadjova
"Infrared spectra of NH_4^+ ions matrix-isolated in Tutton compounds $M_2'M''(XO_4)_2\cdot 6H_2O$ (M' = Rb, Cs; M'' = Mg, Co, Zn; X = S, Se)"
American Chemical Science Journal, 5(3), 2015, 202-213.

Infrared spectra of ammonium doped rubidium and cesium sulfate and selenate matrices, $M'_2M''(XO_4)_2\cdot 6H_2O$ (M' = Rb, Cs; M'' = Mg, Co, Zn; X = S, Se), are presented and discussed in the region of both the asymmetric bending modes ν_4 of the ammonium ions and water librations. The ammonium ions included in the sulfate matrices display three bands corresponding to n_4 in agreement with the low site symmetry C_1 of the host cations, while those included in the selenate matrices exhibit four bands for ν_4. A hypothesis is made that the reason for this phenomenon is the formation of polyfurcate hydrogen bonds between the ammonium guest ions and the selenate host ions, thus leading probably to a disorder of the ammonium ions. The degree of energetic distortion of the ammonium ions with respect to the bond angles H−N−N as deduced from the values of $\Delta\nu_4/\nu_c$ depends on the repulsion potential of the matrices and the strength of the hydrogen bonds.

The strength of the hydrogen bonds formed in the rubidium and cesium salts containing isomorphously included ammonium ions as deduced from the wavenumbers of the water librations is discussed. The analysis of the spectra reveals that weaker hydrogen bonds are formed in the mixed crystals $M'_{1.85}(NH_4)_{0.15}M''(XO_4)_2\cdot 6H_2O$ (M' = Rb, Cs; M'' = Mg, Co, Zn; X = S, Se) as compared to those formed in the neat rubidium and cesium compounds. These spectroscopic findings are owing to the decrease in the proton acceptor strength of the SO_4^{2-} and SeO_4^{2-} ions as a result of the formation of hydrogen bonds between the host anions and the ammonium guest cations (*anti*-cooperative or proton acceptor competitive effect).

Keywords: Tutton compounds, $M'_2M''(XO_4)_2\cdot 6H_2O$ (M' = Rb, Cs; M'' = Mg, Co, Zn; X = S, Se), Matrix infrared spectroscopy, Matrix-isolated NH_4^+ ions, Water librations.

Publication 26C

V. Karadjova, M. Wildner, D. Stoilova

"Infrared spectroscopic study of $Cs_2Ni(XO_4)_2\cdot6H_2O$ (X = S, Se) and of NH_4^+ ions included in $M_2Ni(XO_4)_2\cdot6H_2O$ (M = Cs, Rb; X = S, Se) and Crystal Structures of $(M, NH_4)_2Ni(XO_4)_2\cdot6H_2O$ (M = Rb, Cs; X = S, Se) Mixed Crystals"

International Research Journal of Pure and Applied Chemistry, 5(3), 2015, 245-262.

The solubility in the three-component Cs_2SO_4-$NiSO_4$-H_2O system was studied at 25°C by the method of isothermal decrease of supersaturation. It has been established that a double salt, $Cs_2Ni(SO_4)_2\cdot6H_2O$, crystallizes from the ternary solutions within a wide concentration range.

Infrared spectra of neat Tutton compounds $Cs_2Ni(XO_4)_2\cdot6H_2O$ (X = S, Se) as well as those of ammonium doped rubidium and cesium sulfate and selenate matrices are presented and discussed with respect to the normal modes of the tetrahedral ions and water librations. The ammonium ions included in the sulfate matrices exhibit three bands corresponding to the asymmetric bending modes n_4 in agreement with the low site symmetry C_1 of the host cesium and rubidium cations. However, the inclusion of ammonium ions in the rubidium and cesium selenate structures leads to the appearance of four bands in the region of n_4 of the ammonium ions. At that stage of our knowledge we assume that some kind of disorder of the ammonium ions included in the selenate lattices occurs due to the strong proton acceptor capability of the SeO_4^{2-} ions (stronger than that of the SO_4^{2-} ions), thus facilitating the formation of polyfurcate hydrogen bonds by the ammonium ions in the selenate matrices.

The strength of the hydrogen bonds formed in the mixed crystals $M_{1.85}(NH_4)_{0.15}Ni(XO_4)_2\cdot6H_2O$ (M = Rb, Cs; X = S, Se) as deduced from the frequencies of the water librations is discussed. The spectroscopic experiments reveal that the water molecules in the mixed crystals form weaker hydrogen bonds than those in the neat rubidium and cesium Tutton salts due to decreasing in the proton acceptor strength of the SO_4^{2-} and SeO_4^{2-} ions as a result of the formation of hydrogen bonds between the host anions and the NH_4^+ guest cations (*anti*-cooperative or proton acceptor competitive effect).

Crystal structure investigations of several $(M, HN_4)_2Ni(XO_4)_2\cdot6H_2O$ (M = Rb, Cs; X = S, Se) mixed crystals reveal significant changes in the environment of the monovalent cations as well as in the hydrogen bonding systems of the water molecules upon incorporation of ammonium ions. Disorder of NH_4 groups and the formation of polyfurcate N–H···O hydrogen bonds have not been observed, but neither can be excluded by the X-ray diffraction experiments, especially not for rather low ammonium contents.

Keywords: Tutton compounds, $Cs_2Ni(XO_4)_2\cdot6H_2O$ (X = S, Se), Solubility diagram, Infrared spectra, Matrix-isolated NH_4^+ guest ions, Water librations, Crystal structures

Publication 27C

T. Petrova, **V. Karadjova**, L. Fachikov, J. Hristov
“Silver recovery from spent photographic solution by natural magnetite: Attempts to estimate the process mechanisms and optimal process conditions”
International Review of Chemical Engineering vol. 4, 3, 2012, 373-378.

Spent solutions from classic photographic processes have been used for cementation of silver onto natural magnetite sand. The effects of the solid phase content, initial pH of the solution, modified by sulphur acid, on the amount of silver recovered have been studied. Some ad hoc experiments were performed by treatment with 76% selenic acid as well as telluric acid. The silver deposits depend on the pH of solution (sulphur acid treatment) and the type of acid used. The sulphur acid treated solutions allow silver deposits mainly close to the magnetite surface as thin flat deposits, while those treated by selenic and telluric acids results in enormous amounts of star-like dendrites.

Keywords: Silver Recovery, Spent Photographic Solutions, Deposit Shape, Cementation, Magnetite