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RESEARCH ARTICLE

An Alternative Method to Assessment on Safety Effectiveness of Food Additives

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ABSTRACT

The active sites of enzymes that interact with chemicals are three-dimensional and optically active. Taking into consideration the properties of catalytic sites, it is considered that determining the geometric properties of the chemical substances and the functional groups that they have might make a contribution to the assessment of the safety of food additives. To obtain the toxicological data of chemicals is a time-requiring and challenging process. Since the number of chemical compounds is significantly high, it is not possible to perform toxicological assessment for each. Therefore, it is important to predict if toxic or not by using the formulas of chemical compounds. In this study, differences between the geometric structures of chemical compounds (control group) constituting the nutrients were analyzed in terms of consumption and those of food additives added into the food in order to have aroma, flavor and color, by means of group theory. This study aims to predict if food chemicals can be toxic or not using point group analysis. As a material, molecules consisting of food additives, chemical formulas of amino acids, sugars, fatty acids, and secondary metabolites and additives used to regulate the properties of foods have been used in the study. Two and three-dimensional structures of these formulas have been drawn and point groups have been determined. As a method, Campus-licensed versions of ChemDraw 19.0 and Gaussian 09W have been used to draw two and three-dimensional structures of formulas and to carry out the molecular calculations respectively, which are presented by our University. GaussView 6.0 (Free) has been used to analyze the geometrical properties of the molecules based on Group Theory.

Contents

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1. Introduction

With The spectroscopic properties and molecular orbitals of the compounds are explained by means of the structure of molecules with group theory. The theory is used for the theoretic explanation of the results obtained experimentally.

Enzymes catalyze the chemical reactions in living systems. The structure of the catalytic concentrates in enzymes is three-dimensional. Therefore, molecules with particular geometrics can approach enzymes and each enzyme has an impact on specific functional groups. After the chemicals used in the food enter into our body interact with enzymes to be used or destructed. Reactions catalyzed by enzymes occur in a three-dimensional region called an active center on the enzyme. The molecule held by this center and affected by the enzyme is called the substrate [1].

Determining the geometric properties of chemicals and their functional group similarities by using the constraints in the catalytic regions can make a contribution to the assessment of the safety of food products.

Chemical compounds that develop or adjust the properties such as color, appearance, flavor and odor of food are called food additives. Additives are added into foods in order to provide various benefits such as extending the shelf life of foods, preventing health risks, reducing losses and preserving their nutritional value. There are a great variety of food additives and the majority of these additives consist of sweeteners and extracts [2, 3].

Since food additives obtained naturally or synthetically are frequently used, it is highly probable that they will interact with the biological systems in our body and create risk. In the researchers conducted, it has been detected that some food additives are genotoxic and carcinogenic, and some play a role in the formation of hyperactivity, allergy, neurodegenerative diseases, obesity, diabetes, reproductive and gastrointestinal system disorders, and their usage has been limited [3].

The assessment of the safety of food additives is carried out by animal experiments. Chemicals that do not pose a risk under normal exposure conditions and/or have a long-term history of safe use are allowed to be used as food additives [2].

USA imposed a prior consent requirement for food additives in the 1950s, the Amendment on Food Additives entered into force in 1958, and it was accepted in USA that food additives should be assessed to assure that they are safe and secure to be used [4, 5]. The audit for food additives is conducted by American Food and Drug Administration (FDA) under the Law on Federal Food, Drug and Cosmetics in USA [5–7].

In USA, direct food additives are legally classified into eight categories Food preservatives; coatings, films and related substances; special dietary and nutritional additives; anticaking agents; flavoring agents and related substances; and secondary food additives divided into four categories: polymer substances and polymer adjuvants for food treatment; enzyme preparations and microorganisms; solvents, lubricants, release agents and related substances; and specific usage additives [2, 5].

Many food additives began to be used long before the comprehensive food laws had been accepted in the US, such as the Food, Drug and Cosmetics (FD and C) that was accepted in 1958. These substances are considered as GRAS based on their safe usage story. GRAS list of FDA includes more than 600 chemical substances.

Food additives legislation of the European Union (EU) ensures the protection of public health in the EU market. General framework legislation no 1331-2008 which serves as a mutual authorization procedure for food additives, good enzymes and food flavors were accepted in December 2008. The current substance lists approved for use in foods in the EU has been updated with the EU commission regulation no 234-2011. The method to evaluate the information necessary for the risk assessment including the legal use of chemicals to be used as food additives, safety information, safety technical information, biological and toxicological data, information on recommended uses, normal and maximum use levels and dietary exposure estimates has been explained by this regulation [8].

Safety assessment is the assessment report that should be carried out in the finished product based on the toxicological property, chemical structure and exposure levels of the compounds of a food product, and the specific exposure characteristics of the target population or product which the product is offered for [9].

Toxicology is the scientific discipline studying the negative impacts of chemical substances on living organisms. It is interested in all foreign substances including drugs taken from outside by various means that are not necessary for the normal metabolism of the organism, which are also known as xenobiotics. Toxicity is the toxic effect of xenobiotics [10].

The main factor which has a determinant impact on the toxicity is the dosage. The expression of LD50 (Lethal Dose) is used as the acute toxicity unit when expressing the toxicity level of a substance. NO(A)EL (No Observed Ad- vers Effect Level), LO(A)EL (Lowest Observed Adverse Effect Level), SED (Systemic Exposure Dose), LC50 (Median Lethal Concentration), QRA (Quantitative Risk Analysis) and MoS (Margin of Safety) are the other toxicity units [11].

JECFA (Joint FAO-WHO Expert Committee Report on Food Additives) serves as a toxicological assessment unit regarding the food accepted to determine the amount of Acceptable Daily Intake (ADI) which refers to the amount that a chemical can be exposed to on a daily basis during a lifetime without any significant risk through food [2, 5, 12, 13].

FDA (Food and Drug Administration), EFSA (European Food Safety Authority) and JECFA made it mandatory to assess the toxicity of food additives. In toxicological studies, animal experiments designed in accordance with the Organization for Economic Cooperation and Development (OECD) and EU guidelines are demanded while information obtained from human studies are accepted as well [8, 14].

2. Experimental

In this study, 143 molecules used in foods and molecule formulas of 121 chemical substances used in living metabolism and as control group have been used as material. The structures of these formulas have been drawn and point groups have been determined.

2.1. Selection of molecules

When selecting the food additives to be worked on, 143 chemical substances included in the GRAS list of FDAs and which do not have polymeric structure and inorganic structure have been preferred [15–18].

121 molecules used in living systems and released as the result of food digestion have been chosen as the control group for comparison purposes. These molecules are amino acids, carbohydrates, fatty acids, vitamins, etc. are molecules.

2.2. Drawing the molecule structures

Molecules of which names are provided in the below tables have been drawn as two-dimensional by ChemDraw 19.0 and saved in CDX. And, the CDX file has been opened with ChemDraw 3D and saved in *GJF. When determining the point groups, these GJF files have been used by Gaussian 09W and GaussView 6.0 programs.

2.3. Obtaining ADI values

ADI values of the molecules have been obtained from https://apps.who.int/food-additives-contaminants-jecfa-database/search.aspx/ on Internet.

2.4. Principles to consider when examining molecules

Molecules have been examined according to Group Theory with a set of principles called “Hatko Principles” developed by Prof. Dr. Yaşar Demir in order to have standardization in the examination of cosmetic products based on Group Theory [19].

2.5. Programs used in examination of molecule structure

GaussWiev 6.0 has been used in determining the point groups of molecules. After the GJF file has been opened, a sub-window has been opened when clicked on “Tools>Point Group…>” command. And when “Enable Point Group Symmetry” on the left top corner of the window is marked, the existing point group of the compound has been viewed in the field of “Current point group”.

3. Results and Discussion

As a result of the examinations and researches carried out, point groups based on Group Theory and Acceptable Daily Intake (ADI) values have been determined separately.

3.1. Point group analysis

In the examination performed according to Group Theory, 143 chemical molecules consisted of food additives and 121 chemical molecules consisted of nutrients (control group) have been examined. As a result of these examinations, the following data have been obtained.

Table 1 Molecular numbers and percentages of food additives and control group examined based on the Group Theory.

Groups	Control Group		Food Additive	
	Number	%	Number	%
CS	87	71.90	97	67.83
C1	32	26.45	30	20.98
C2v	1	0.83	12	8.39
C2h	1	0.83	4	2.80

When Table 1 is examined to see the differences between the groups, it is seen that the molecules of the control group and the food additives are clustered in four different point groups. Cs, C1, C2v and C2h point groups are seen in both clusters.

The point group where the molecules cluster the most in both groups is the CS group according to the in-group analysis. The second group where the molecules cluster is the C1 point group. C1 point group points out that the molecule has inversion. The Cs point group points out that the molecule has one inversion process and one axis of symmetry. C2v points out that there is one axis of symmetry and a plane of symmetry vertical to the axis while C2h points out that there is one axis of symmetry and a plane of symmetry parallel to this axis.

When the distribution of point groups is examined, it is seen that the active sites of most enzymes working with food chemicals do not have a fixed geometric structure, which shows that activation mechanisms of enzymes are more suitable for the Interaction Resulted Conformity model.

When the percentages of these group members are compared to each other (Additives / Control Group), “Incidence Frequency, (GSx)” of these features are obtained. The Incidence Frequency is given in Table 2.

Table 2 Incidence Frequency (GSx) of point groups determined based on Group Theory.

Point Groups	Incidence Frequency (GSx)
CS	1.060
C1	1.261
C2v	0.098
C2h	0.295

Cs and C1 groups having high GSx values means that food additives mostly do not have a stable geometry.

3.2. Analysis of acceptable daily intake (ADI) values

The examination of both ADI in the GRASS list, control group, and that of monomers have been carried out by means of https://apps.who.int/food-additives-contaminants-jecfa-database/ search.aspx of World Health Organization.

It could not be found that the use of any of the molecules studied is undesirable.

According to the data obtained, it seems possible to predict if chemical substances are harmful or not by means of Group Theory. If the point group of any molecule is one of Cs, C1, C2v or C2h point groups, the molecule can be considered to have a high possibility to be used as a food substance.

In this estimation process, it seems reasonable to compare the point groups of food additives with the molecules found in foodstuffs or released as a result of nutrients digestion. This assumption seems correct, as nutrients and the monomers that make up them are used as building blocks or energy components in cells.

4. Conclusion

According to the data obtained in this study, it is possible to produce a conclusion about whether they are beneficial or harmful by determining the point groups with the help of the formulas of additives used in food products.

Author Contributions

YD, ND and HN conceived of the manuscript. YD, ND, HN and MU conducted the analysis of food additives. YD analyzed the data and the article was prepared with the contributions of all authors. All authors have read and approved the final version of the article.

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Ethics Statement

This article reports on developing an analysis method for food additives that does not require ethical clarity.

Conflict of Interest

The authors declared no conflict of interest.

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