IMPACT OF TOXICOLOGY ON FOOD PROCESSING

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Edited by

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Preface

This symposium on the Impact of Toxicology on Food Processing was the fourth in the series of basic symposia on a topic of major importance to food scientists and food technologists. The symposium, sponsored by the Institute of Food Technologists and the International Union of Food Science and Technology, was held June 6–7, 1980, immediately prior to the 40th Annual IFT Meeting. It was so planned to provide an up-to-the-minute status of food safety issues and to provide the framework for proceedings that would be of importance and of current interest to anyone involved in the development, production, packaging, and distribution of food products.

The symposium was organized into four sections, each presented in a half-day session. The first section defined terms, outlined parameters, and delineated what toxicology embraces, its impact on regulatory practices, the role that government agencies take in their function as regulators, the costs that such regulation engenders, the benefits derived, and finally some effects of food processing that result in the formation and destruction of toxic constituents in various commodities.

The second session dealt with a number of unwanted biological substances in foods, beginning with enzyme inhibitors and followed by plant produced cyanogenetic glycosides. Toxins of algal, fungal, and microbial origin were each discussed separately.

The second day was devoted to the consideration of chemical substances in foods and to factors that enhance food processing and preservation. In the morning, consumer responses such as hypersensitivity, flatus, and intolerance were evaluated, and the role of pesticides and of various condiments elucidated.

The last session was devoted to a discussion of the possible toxicity of certain vitamins, colors, processing aids, fillers, and irradiated foods, and an overview of regulatory and safety assessments that pertain to food

packaging. A few summary remarks from Drs. Ayres and Kirschman concluded the program.

Planning and execution of this Basic Symposium has truly been an impressive joint effort on the part of scientists from industry, government, and academia. The important role of the Basic Symposium Committee—Dr. J.R. Whitaker, Dr. D. Ashton, Dr. G.E. Inglett, Dr. G.A. Leveille, Dr. J.M. McIntire, and Dr. O. Silberstein—is gratefully acknowledged.

The success of the fourth basic symposium was also the result of the expert assistance of Calvert L. Willey, Executive Director of IFT; John B. Klis, Director of Publications, and the IFT staff who helped provide publicity for the symposium, coordinated registration, and took care of the many details of arrangements for meeting rooms, hotel reservations, and numerous other details that go into a successful meeting.

John Klis also served as coordinator and Anna May Schenck, JFS Assistant Scientific Editor, as copy editor for publication of the manuscripts presented at the symposium and it is through their patience and persistence that this monograph has come to fruition.

Success of the Symposium is also due to the excellent cooperation of the many food companies who provided financial assistance as well as moral support. To these companies we are deeply indebted:

Archer Daniels Midland Co., Decatur, Ill.
Armour Food Co., Scottsdale, Ariz.
Beatrice Foods Co., Chicago, Ill.
Beatrice Foods Co., Special Products Div., Chicago, Ill.
Best Foods, CPC International, Englewood Cliffs, N.J.
Californian & Hawaiian Sugar Co., Crockett, Calif.
Campbell Soup Co., Camden, N.J.
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Hershey Foods Corp., Hershey, Pa.
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Kraft, Inc., Glenview, Ill.
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The Pillsbury Co., Minneapolis, Minn.
The Proctor and Gamble Co., Cincinnati, Ohio
The Quaker Oats Co., Barrington, Ill.
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The Seven-Up Co., St. Louis, Mo.
Standard Brands, Stamford, Conn.
Stouffer Foods, Solon, Ohio
Sunkist Growers, Ontario, Calif.
Wm. Underwood Co., Westwood, Mass.
Universal Foods Corp., Milwaukee, Wisc.

Indeed, the seed of the idea of an annual basic symposium planted in the fall of 1974 has survived the winters of uncertainty and doubt and has sprung forth once again to bear fruit . . . making a worthwhile contribution to our knowledge of food science and technology.

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December, 1980

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Contents

PREFACE v

1 Definition of Toxicology and Physiological Effects 1
John C. Kirschman

2 Role of Toxicity in Regulatory Practice 4
R.W. Fogleman

3 Government and Its Influence on Toxicology 17
Albert C. Kolbye, Jr.

4 Benefits and Costs of Food Additive Regulations 28
Dee M. Graham

5 Effect of Food Processing in the Formation and Destruction of Toxic Constituents of Food 35
C.O. Chichester and T-C. Lee

6 Naturally Occurring Peptide and Protein Inhibitors of Enzymes 57
John R. Whitaker

7 Unwanted Biological Substances in Foods: Cyanogenic Glycosides 105
Eric E. Conn

8 Unwanted Biological Substances in Foods: Aflatoxins 122
Urban L. Diener

9 Impact of Microorganisms and Their Toxins on Food Processing 151
E.M. Foster

10 Significance of Hypersensitivity Reactions to Chemicals in Foods 162
H. Tryphonas
11 Unwanted Sugars in Processed Foods 177
T.O.M. Nakayama
12 Impact of Toxicology on the Availability of Pesticides for Use in the Production of Food 194
John L. Emmerson
13 Antibiotics 206
Beverly A. Friend and Khem M. Shahani
14 The Safety of Antioxidants—Fact or Fallacy 224
J.W. Daniel
15 Condiments, Spices, and Flavors 237
Richard L. Hall
16 Vitamins in Food: Implications for Quality and Toxicity 251
K.C. Hayes
17 Toxicity and Safety Requirements of Colors 261
John C. Kirschman
18 Bulking Agents and Fillers 273
John J. Beereboom
19 Irradiated Foods—Are They Safe? 286
J.F. Diehl
20 Food Packaging: An Overview of Regulatory and Safety Assessments 305
Robert M. Miller
Index 311

1

Definition of Toxicology and Physiological Effects

John C. Kirschman[1]

It is critical that scientists responsible for maintaining a safe and wholesome food supply understand the forces at work which now and in the future will affect the ways of assessing and assuring food safety.

As soon as one starts talking about toxicity he is shortly stumbling through the various disciplines of the biological sciences including pharmacology, physiology, anatomy, biochemistry, nutrition, cytology, and pathology. Indeed, the practice of toxicology involves all of these disciplines and then some—more recent additions are genetics, epidemiology, allergenicity and hypersensitivity, and behavior—perhaps law and public relations should be added as well. We dare not compartmentalize our thinking or research when addressing food safety issues since they all must be considered in every case.

Let's consider that the subject of concern, be it human or animal, is an operating chemical plant—which it is. Our objective is to keep it operating efficiently and economically as long as possible. In order to do so we need to know the potential limiting factors and the dynamics of their interaction. Production at the plant can be adversely affected—toxicologically—in a variety of ways. For example, it depends upon:

1. Structural adequacy	(Anatomy)
2. Availability—scarcity or over-abundance—of materials	(Nutrition)

[1] General Foods Corporation, White Plains, New York.

3. Adequate maintenance	(Physiology and Nutrition)
4. Proper plant design—work flow	(Pharmacology)
5. Equipment capacities and maintenance	(Pathology)

Since the ultimate visible impact on the plant will be the same from a variety of causes, it is important to understand the qualitative and quantitative aspects leading to the endpoint of toxic phenomena and some insight into mechanism of action must be determined and taken into account in evaluating toxicity test results for use in risk assessment. Only in this way can one properly begin to establish their relevance to safety in use for man. For example, simple reading of endpoints such as incidence of test animal deaths at a given exposure level, can yield very accurate data yet generate incorrect conclusions.

Extremely high chemical doses for prolonged chronic exposure can elicit toxicological effects by poisoning a system directly or secondarily by overloading normal functions or inducing nutritional deficiencies, conditions that would not obtain at lower ranges of exposure rates.

By preventing absorption of or using up all of available nutrients (*e.g.*, GSH, Zn) during metabolism, exceedingly high test chemical doses could cause responses not shown in the control animals where the diet is nutritionally adequate in the absence of a chemical overload. In such cases there might have been a control group in the study yet the study was not properly controlled. Thus the observed test response should be considered a secondary one resulting from an imposed nutritional deficiency rather than a specific toxic effect of the chemical. Such factors are a key part of the discussion in recent years about the use of NCI's bioassay data for making determinations of risk to man.

As we start reviewing the safety of materials already in our foods and long generally considered as safe (GRAS), and materials designed as replacements for normal components of foods, there develops an increasing need and opportunity for interdisciplinary approaches to the problem.

The toxicologist must involve the nutritionist, clinician, epidemiologist and biochemist earlier in the study planning than ever before. It has been said for test protocol design, "As with an obstetrician, the statistician should be brought in before the labor begins." As we start testing materials with nutritional value (*e.g.*, irradiated foods, modified ingredients) we must bring in the nutritionist and biochemist earlier than ever before.

Whenever one is able to acquire data on the toxicological and biochemical characteristics of a chemical *in man*, it is important to do so for help

in designing and interpreting the animal studies. This should be possible more often with food ingredients already in use than with new xenobiotic (strange to biological systems) chemicals. Without such information one must presently rely solely on animal data and the conservative approach of setting an Acceptable Daily Intake (ADI), for example, by applying a 100-fold safety factor to the highest no observed effect level in the most sensitive test species. Most foods would not survive this rigid procedure.

Additional attention in the future will be focused on products of reactions between additives and nutrients or other food constituents during manufacture, storage and preparation for serving. This need will also mandate closer than ever working relationships between toxicologists and analytical chemists.

After adding to these opportunities the galloping snail of advancing toxicology (*e.g.*, genetic tox, allergenicity, hyperactivity, behavior) we have an exciting era ahead of us in the arena of Food Safety.

2

Role of Toxicity in Regulatory Practice

R. W. Fogleman[1]

Toxicology is a multi-disciplinary application of scientific knowledge to the problems of hazard assessment. Therefore, by definition, toxicology is the receiver of the input of knowledge of many scientific disciplines and applies these facts, phenomena, laws and proximate causes, gained and verified by exact observation, organized experimentation and ordered thinking to define the conditions under which a product may be used safely. The role of the toxicologist is to discover the limits within which a chemical may be used safely, *i.e.*, with minimum risk to the target organism and to all other factors of the ecosystem and environment.

While this may sound simple, there are many complicating factors which represent specific concepts of hazard or risk, specific concepts of social acceptability, personalities, power structures, and economic considerations, which impact on what should otherwise be a scientific process. This paper will examine both the technical and the nontechnical aspects of toxicology and its role in Regulatory Practice.

FACTORS ENTERING INTO A TOXICOLOGICAL PROBLEM

Many factors enter into a toxicological problem; the most important considerations are:

1. What are the exposure conditions?
2. How much?
3. What are the effects—both good and bad?
4. Benefit/Risk.
5. Public Relations.

[1] Consulting Toxicologist, Upper Black Eddy, Pennsylvania.

What Are the Exposure Conditions?

How is the chemical to be used? For example, a food additive to be used in the preparation of bread represents one set of conditions whereby a large number of humans and animals will be exposed, probably for long periods of time, and there are no limits on age, *i.e.*, small children, the infirm and aged will also be exposed. On the other hand, a drug to be administered once or at most only a few times to a defined population under close supervision of a well qualified physician represents another set of conditions. Obviously there are many shades between these two extremes, but it is essential that the proposed pattern of use be defined so that the exposure can be known.

How Much—of What?

As Paracelsus stated back in the sixteenth century, it is the dose alone that makes a thing a poison. Early in any program, the amount, or quantity of the substance entering into the exposure has a significant impact on planning. Using our example of a food additive in bread, the chemist can supply fairly accurate data on the quantity of the additive that is to be present in the finished product, and the exposure, in terms of probable daily dosage, can be estimated from these and other readily available facts. The same also is true in our drug example, provided the drug is limited to humans. Assuming that same drug is to be given to animals used for human food, other problems are immediately suggested. Residues in the food derived from the treated animal, not only of the parent compound but metabolites and degradation products as well, become important both from a qualitative and quantitative point of view.

What are the Effects?

A preliminary evaluation of the known structure, preliminary data on toxicity, and prior experience with compounds of similar structure point out problem areas and begin to give some insight to the potential risk which might be expected. For example, some structures are associated with known carcinogenic activity, others are known to affect key enzyme systems. Some act rapidly in biological systems, while others are stored for long periods of time.

Benefit/Risk

This is a very controversial subject and much has been written about it (Bazelton 1979; Comar 1979). Obviously a benefit is expected, but for

every benefit there is a potential risk to health, to the environment, and to society. Many factors, many nonscientific, enter into this equation, and it is a very difficult area with which to deal. However, an early assessment is necessary on which to base a decision, and that assessment must be continually updated as the program develops.

Public Relations

This is an odd consideration for a scientific presentation, but it is one that is seriously overlooked by most toxicologists. By way of background, science generally, and toxicology specifically, has a poor reputation among the general public. We have lost credibility and our presentments are not to be trusted. The result is a public fear of "chemicals" and a public demand for their suppression and control. This public fear is being fed by those who capitalize on that fear. Unfortunately, some scientists are guilty of this practice, too. They are easily recognized, however, by the discerning observer who notes that these individuals publish their findings in such illustrious journals as *The New York Times* and are immediately funded by large private or government grants.

Another area of concern involving public relations hinges on the fact that the interpretation of toxicologic data is a "negative" science, in that we attempt to demonstrate that a given event will not occur. As a result we must deal in probabilities, not absolutes; and the public has been carefully conditioned to accept absolutes. The "buzz-words" today are "might," "could," "under some conditions," "it is possible," or "in the absence of data," coupled with the words "cancer" and "birth defects." The public has also been conditioned to accept the proposition that the resolution of all doubt is the result of a new study, more money, a new bureau, and more time.

Knowing these conditions, the toxicologist must examine his conscience and select his path. As I have already unhappily noted, some of our colleagues have opted for the short-term funding approach at the expense of the consumer, science, and their own reputations.

ROLE OF THE TOXICOLOGIST

In examining the role of toxicity, the role of the toxicologist must be carefully considered.

First of all, the toxicologist must be grounded in many disciplines, such as physiology, biochemistry, pharmacology. medicine, mathematics, genetics, immunology, and psychology, to mention a few. In addition, management experience is helpful, because he must deal with the management of money, personnel and facilities as they impact on management decisions.

Observing many organizations, I find toxicologists are being placed high on the decision tree. They serve in staff positions at the highest level, providing the input needed to plan and carry out research projects. In addition, most organizations maintain laboratory facilities, and toxicologists fill these line responsibilities, but the emphasis is on the management role, and it is here that performance is critical.

The same is true in government. Toxicologists provide staff input in the regulatory decisions to the various regulatory agencies.

USE OF TOXICOLOGY LABORATORY SERVICES

To function, the toxicologist must have data that are reliable. The source of the data may be from several types of facility. Any facility must be adequately staffed and equipped to do the job in a timely manner. It may be a part of the research function in industry, a contract toxicology laboratory, a university, or a government laboratory.

A toxicology laboratory is a capital intensive, high technology operation, undergoing constant change. It is expensive to maintain and to operate. A management decision to have a toxicology laboratory involves considerably more thought than deciding to get a few cages. Consider a typical budget for the toxicology studies necessary to evaluate a new food additive.

Typical Costs of Toxicology Studies

Acute and Subacute	$ 7,000 –	$ 50,000
90-Day Rat and Dog	70,000 –	100,000
2-Year Chronic Rat	125,000 –	450,000
18-Month Mouse	200,000 –	350,000
3-Generation Reproduction	100,000 –	150,000
Teratology	35,000 –	70,000
Mutagenicity	4,000 –	50,000
Environmental	10,000 –	150,000
Inhalation	2,000 –	200,000
Special Studies	25,000 –	250,000
	$565,000 –	$1,820,000

Consider also the disciplines required beyond the toxicologist. Essential technical support includes pathologists, biochemists, computer scientists, and other specialists, each with a full complement of technical assistants and equipment. Few, if any, laboratories in industry, government, or academia are staffed and equipped to handle all aspects of a full-blown toxicology evaluation.