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Positron emission tomography in food sciences

Editorial

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Recent progresses in food sciences have led to the development of a range of excellent analytical methods that enable accurate determination of the composition of foods and to study food components and contaminants at both the micro- and macrostructural level. But this does not necessarily tell us enough about the nutritional value or the safety of those foods (Ibanez and Cifuentes, 2001; Prentice et al., 2002). This is because only a fraction of nutrients or other biologically active compounds present in food can be absorbed into the body, and this fraction strongly depends on the type of food and its preparation.

It is therefore important to know how much of a certain substance can be absorbed, what happens to this substance when it enters the body, and, finally, what happens to the body. The interest in these questions steadily increases due to the fact that the design and development of novel foods, genetically modified foods, novel food ingredients and additives, and new methods of food processing is a rapidly evolving field. Furthermore, improved analytical methods and molecular techniques direct our attention to a rapidly growing number of biologically significant substances, including numerous functional food ingredients, 'nutriceuticals', and foodborne toxicants (Martens, 2000; Dwyer and Peterson, 2002; WHO report, 2002; Brent, 2004; Schauzu, 2004; Verhagen et al., 2004; Yokoyama et al., 2004). In this context, experimental approaches *in vitro* offer the advantages of providing rapid results, produced in strictly controlled environments. However, they need to be validated increasingly against *in vivo* studies to make sure that they provide a good prediction of what actually happens in and with the living organism. The latter is a prerequisite to enact new recommendations and regulations, e.g., on novel foods and novel processes.

One tool of choice is functional imaging by positron emission tomography (PET). As far back as the 1950s, positron-emitting radiotracers have been used for localization of brain tumours at the Massachusetts General Hospital. Since the 1980s, PET has become more and more important. This was essentially due to both the rapid development of PET radiochemistry in which many biologically significant molecules could be labelled with PET nuclides and progress in PET physics and technology which contributed to better scanners and image processing, providing higher resolution and sensitivity (Chatziioannou et al., 2001; Schlyer, 2004). At present, PET represents the most selective and sensitive method (at the picomolar to nanomolar level) to depict physiologic, metabolic, and molecular pathways *in vivo* (Jones, 1996; Phelps, 2000a; Phelps, 2000b). Apart from its capacity to provide new pathophysiological information on human disease, PET is also important for the objective assessment of therapeutic efficacy and plays an ever increasing role in pharmaceutical research, e.g., in the development of new drugs (Eckelman, 2002; Paans et al., 2002; Paans and Vaalburg, 2004; Sinskey et al., 2004). In this line, PET also has a high potential as a tool for food sciences providing the opportunity to study pharmacokinetics, pharmacodynamics, and the mode of action of substances of interest present in food in both animal models and humans.

PET is a tomographic imaging modality which allows for accurate non-invasive determination of biochemical and physiological processes *in vivo* in a quantitative way by using tracer compounds labelled with short-lived positron-emitting radionuclides and by measuring the annihilation radiation using a coincidence technique. By using different tracer compounds, a nearly unlimited range of physiological, biochemical, and pharmacokinetic parameters can be measured. Some examples are blood flow (perfusion), oxygen utilisation, glucose metabolism,

receptor density and affinity, enzyme activity, neurotransmitter release, drug delivery and uptake, gene expression, cell proliferation, cell migration, etc. This versatility originates from the fact that, in principle, virtually all biological molecules can be labelled with positron emitters such as carbon-11 ($t_{1/2} = 20.39$ min), nitrogen-13 ($t_{1/2} = 9.97$ min), and oxygen-15 ($t_{1/2} = 2.04$ min) that represent the elements of life (Firestone and Shirley, 1996). In addition, fluorine-18 ($t_{1/2} = 109.77$ min) is often used as a substitute of hydrogen, which itself does not have a positron-emitting isotope. A further assumption behind the labelling of analogues with fluorine-18 is that in many molecules fluorine atoms can be substituted for hydroxy groups often only minorily altering the behaviour of the molecule in the living organism. Due to their short half-lifes, PET radionuclides have to be produced in house with dedicated cyclotrons. Since the chemical form of the cyclotron-produced radionuclides is only simple, e.g., fluorine-18 becomes available as $[^{18}F]F^-$ or $[^{18}F]F_2$, input from both organic chemistry and radiochemistry is essential for syntheses of the desired more complex molecules.

PET is characterised by the ability to measure regional tissue tracer concentrations with high degrees of accuracy and sensitivity. This is based on the specific decay characteristics of positron emitters. In tissue, the emission of a positron and the annihilation of a positron and an electron effectively results in the simultaneous emission of two 511 keV γ-quanta under a relative angle of 180°. These two annihilation photons are emitted in opposite directions and are recorded by coincidence detection (i.e. simultaneous detection by two opposing detectors). These two detectors define the line of response along which the original annihilation took place. As the total path length of both annihilation photons together is also known, accurate correction of the attenuation of the radiation during its passage through tissue is possible.

For kinetic studies the substance of interest itself has to be labelled. After ingestion or intravenous injection of the labelled compound, the distribution of the radioactivity in the different organs and tissues is measured. Using dynamic data acquisition protocols time–activity curves of radioactivity uptake in organs can be derived and the measurements of tissue tracer concentrations can be translated into quantitative values of the tissue function with the help of suitable tracer kinetic models if plasma concentration of the tracer and its metabolites are measured simultaneously by taking blood samples. By varying the labelling position in the molecule, detailed new information can be obtained on the metabolic degradation *in vivo* or on the mode of action. PET can also be applied to predict toxicity. The unrivalled sensitivity coupled with the very high specific activity with which compounds can be labelled leads to applied doses in the picomolar to nanomolar range, several orders of magnitude below pharmacological levels, thus allowing biodistribution studies in man. Information can be obtained on the metabolism, the blood-brain barrier penetration, the receptor occupancy, and specificity of the compound of interest in animal models and humans. Very recently, a lot of small animal models of disease including genetically modified animals have been developed (Bocan, 1998; German and Eisch, 2004; Lyons, 2005). The study of these animals with dedicated small animal PET cameras (spatial resolution of 1^3 to 2^3 mm^3) is likely to provide also new opportunities in food evaluation (Herschman, 2003; Yang et al., 2004; Weber and Bauer, 2004; Roselt et al., 2004).

However, progress can only be achieved when multidisciplinary PET centers closely cooperate with food scientists and food-producing companies and, furthermore, when industry and regulators are recognizing that the use of functional *in vivo* imaging facilitates decision-making whether food components are riskful or, on the other hand, maintain human health. Thus, the main goal of the 1st Workshop on Positron Emission Tomography (PET) in Food Sciences held in Rossendorf (Dresden), Germany, in May 2004 was to instigate a novel discussion forum in this emerging field.

This issue contains, beside an invited review article emphasizing new concepts on biomarkers to assess the effects of dietary exposure, a selection of contributions originally presented at that workshop, under the auspices of the PET Center at the Research Center Rossendorf and the Institute of Food Chemistry at the University of Technology Dresden. After a description of the conceptual idea of positron emission tomography and its multidisciplinary approach, in the first part food scientists specify some of their needs for new experimental tools that allow the *in vivo* assessment of bioavailability, biodistribution, metabolism, and metabolic consequences as well as the safety of food contents. This also includes an evaluation of the toxicological, nutritional, and allergenic potential of these contents. In this line, communications have been selected that deal with various classes of dietary compounds under investigation, including isoprostanes, advanced glycation end products (AGEs), isopeptides, and polyphenols. There is still little information on how much of these biologically significant substances is absorbed from different types of foods, or how food preparation affects their absorption. This is important to know because there is substantial and consistent evidence

that intake, e.g., of AGEs or polyphenols, negatively or positively affects the risk of atherosclerosis and cancer (O'Brien et al., 1998; Collins and Ferguson, 2004; Dwyer and Peterson, 2002; Takeuchi and Yamagishi, 2004). The second part is essentially concerned with methodological aspects of PET reviewing current developments in PET nuclide production and radiochemistry, radiopharmacology, metabolite analysis, and quantitative data aquisition and analysis. In the third part papers have been included in order to provide a selection of original experimental applications of PET in food science. These papers cover new methods of radiolabelling of isopeptides and polyphenols, as well as of oxidatively modified proteins and lipoproteins. Furthermore, the use of these novel tracers in dynamic small animal PET studies is demonstrated.

This issue is intended to familiarize and to concern the reader with a promising field of interdisciplinary research. We hope that these proceedings will provide insight into the possibilities of the PET methodology and will encourage researchers in the field of food sciences to think about applications of PET in their specific areas. On behalf of the organizers of the 1st Workshop on Positron Emission Tomography (PET) in Food Sciences, the editor (J.P.) expresses his gratitude to Prof. Gert Lubec, Editor in Chief, for the opportunity given to prepare this special issue of *Amino Acids*. Finally, we thank all the authors for their contribution to this issue.

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