



Chitosan-based systems for molecular imaging[☆]

Prashant Agrawal^{*}, Gustav J. Strijkers, Klaas Nicolay

Biomedical NMR, Department of Biomedical Engineering, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands

ARTICLE INFO

Article history:

Received 17 June 2009

Accepted 29 September 2009

Available online 25 October 2009

Keywords:

Chitosan

Molecular imaging

Imaging techniques

Imaging agents

MRI

CT

Ultrasound

Optical imaging

ABSTRACT

Molecular imaging enables the non-invasive assessment of biological and biochemical processes in living subjects. Such technologies therefore have the potential to enhance our understanding of disease and drug activity during preclinical and clinical drug development. Molecular imaging allows a repetitive and non-invasive study of the same living subject using identical or alternative biological imaging assays at different time points, thus harnessing the statistical power of longitudinal studies, and reducing the number of animals required and cost. Chitosan is a hydrophilic and non-antigenic biopolymer and has a low toxicity toward mammalian cells. Hence, it has great potential as a biomaterial because of its excellent biocompatibility. Conjugated to additional materials, chitosan composites result in a new class of biomaterials that possess mechanical, physicochemical and functional properties, which have potential for use in advanced biomedical imaging applications. The present review will discuss the strengths, limitations and challenges of molecular imaging as well as applications of chitosan nanoparticles in the field of molecular imaging.

© 2009 Elsevier B.V. All rights reserved.

Contents

1. Introduction	42
2. Chitosan	43
3. Molecular imaging	45
3.1. Imaging techniques	45
3.1.1. Computed tomography (CT)	45
3.1.2. Magnetic resonance (MR)	45
3.1.3. Positron emission tomography (PET)	46
3.1.4. Single photon emission computed tomography (SPECT)	46
3.1.5. Ultrasound (US)	46
3.1.6. Optical imaging (OI)	47
3.1.7. Imaging mass spectroscopy (IMS)	47
3.2. Imaging agents	47
3.2.1. Nanoparticle-based imaging agents	48
3.2.2. MRI contrast agents	49
4. Current status of the use of chitosan composites in bioimaging applications	51
5. Conclusions	55
Acknowledgements	56
References	56

1. Introduction

Chitosan [poly(1,4-β-D-glucopyranosamine)], an abundant natural biopolymer, is produced by the deacetylation of chitin obtained from the shells of crustaceans. It is a polycationic polymer that has one amino group and two hydroxyl groups in the repeating hexosaminide residue (Fig. 1). Chitosan has great potential as a biomaterial because

[☆] This review is part of the *Advanced Drug Delivery Reviews* theme issue on "Chitosan-Based Formulations of Drugs, Imaging Agents and Biotherapeutics".

^{*} Corresponding author.

E-mail address: p.agrawal@tue.nl (P. Agrawal).

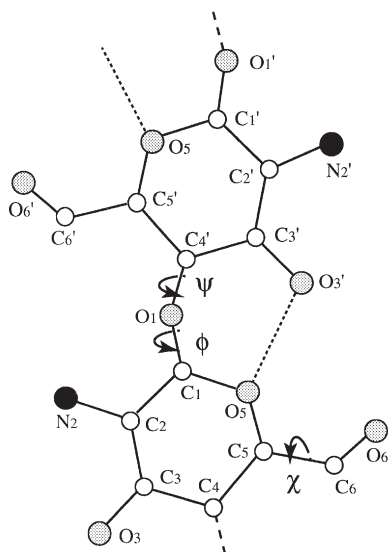


Fig. 1. Chemical structure of chitosan. Individual atoms are numbered. Dashed lines denote O3—O5 hydrogen bonds. Two dihedral angles (φ , ψ) defining the main chain conformation and one dihedral angle χ defining the O6 orientation are indicated.

of its bio-compatible properties. It is hydrophilic, non-antigenic and has a low toxicity toward mammalian cells [1–3]. In addition, chitosan is known to facilitate drug delivery across cellular barriers and transiently open the tight junctions between epithelial cells [4,5]. Chitin and chitosan are aminoglucopyrans composed of N-acetylglucosamine (GlcNAc) and glucosamine (GlcN) residues. These polysaccharides are renewable resources which are currently also being explored intensively for their applications in pharmaceutical, cosmetics, biomedical, biotechnological, agricultural and food industries [1,6].

These polymers have emerged as a new class of physiological materials of highly sophisticated functions and to exploit the properties of these versatile polysaccharides, attempts are being made to derivatize them [7]. Chemical modifications have done an excellent job for the preparation of chitosan derivatives with higher solubility in water, such as O-N-carboxymethyl-chitosan, [8] N-carboxymethyl-chitosan, [9] O-carboxymethyl-chitosan, [10,11] N-sulfate-chitosan, [12] O-sulfate chitosan, [13] O-succinyl-chitosan, [14] N-methylene phosphonic chitosan, [15] hydroxypropyl chitosan, [16] N-trimethyl chitosan, [17] and others. The emergence of synthesis strategies for the fabrication of nanosized particles leads to advancements in the nanotechnology, which benefits molecular imaging for understanding of biological processes at the molecular level. In addition, with the added multi-functional features such particles may become an integral part of the development of next generation therapeutic, diagnostic and imaging technologies.

Molecular imaging holds the promise of the non-invasive assessment of biological and biochemical processes in living subjects. Since the inception of X-ray technology for medical imaging, many non-invasive methodologies have been invented and successfully used for applications ranging from clinical diagnosis to research in cellular biology and drug discovery. Such technologies therefore have the potential to enhance our understanding of disease and drug activity during preclinical and clinical drug development. The advantage of molecular imaging techniques over more conventional readouts (e.g. immunohistochemistry) is that they can be performed in the intact organism with sufficient spatial and temporal resolution for studying biological processes *in vivo*. Furthermore, molecular imaging allows a repetitive and non-invasive study of the same living subject using identical or alternative biological imaging assays at different time points, thus harnessing the statistical power of longitudinal studies, and reducing the number of animals required and cost.

Molecular imaging usually exploits specific molecular probes as well as intrinsic tissue characteristics as the source of image contrast, and provides the potential for understanding of integrative biology, earlier detection and characterization of disease, and evaluation of treatment [18]. Molecular imaging could also aid decisions to select promising drug candidates that seem most likely to be successful or to halt the development of drugs that seem likely to ultimately fail [18].

Different imaging techniques are, in general, complementary rather than competitive and the choice of imaging modality depends primarily on the specific question that has to be addressed (Fig. 2). Imaging of biological specimens both *in vitro* and *in vivo* has long relied on light microscopy (fluorescence and luminescence imaging). The presently leading non-invasive imaging techniques are computed tomography (CT), magnetic resonance (MR), positron emission tomography (PET), single photon emission CT (SPECT), ultrasound (US) and optical imaging (OI), including their variations and sub-categories [19–25]. Biomedical imaging research has prospered in recent years because of the significant advances in electronics, information technology and, more recently, nanotechnology.

The above imaging modalities can be broadly divided into two groups, i.e., morphological/anatomical and molecular (i.e. functional) imaging techniques. The morphological/anatomical imaging technologies, such as computed tomography (CT), MRI and ultrasound (US), are characterized by high spatial resolution (Fig. 2). However, they also share the limitation of not being able to detect diseases until structural changes in the tissue (for example, growth of a tumor, or extent of inflammation) are large enough to be morphologically detected. On the other hand molecular imaging modalities, such as optical imaging, PET and SPECT, offer the potential to detect molecular and cellular changes caused by disease (for example, before the tumor is large enough to cause structural changes). However, these molecular modalities suffer from a poor spatial resolution with currently available technology and do not provide anatomic information (Fig. 2).

The present review will discuss the strengths, limitations and challenges of molecular imaging as well as applications of chitosan nanoparticles in the field of molecular imaging. We will first explain the properties of chitosan, then will discuss different strategies of molecular imaging, including their advantages and disadvantages. In the last part of this review, agents for imaging will be reviewed as well as the potential role and application of chitosan as a constituent of molecular imaging contrast agents.

2. Chitosan

Chitosan is a natural polysaccharide derived from chitin and it has been frequently employed as a polymer for self-assembling nanoparticles (Fig. 1). Most commonly, chitin represents the skeletal material of invertebrates. R-Chitin occurs in the calyces of hydrozoa, the egg shells of nematodes and rotifers, the radulae of mollusks, and the cuticles of arthropods, while α -chitin is part of the shells of brachiopods and mollusks, the cuttlefish bone, the squid pen, and the pogonophora tubes [1]. Chitin is also found in exoskeletons, peritrophic membranes, and cocoons of insects. All these organisms synthesize chitin according to a common pathway that ends with the polymerization of N-acetylglucosamine from the activated precursor UDP-GlcNAc [1].

The industrial preparation of chitin uses the shells of crabs, shrimps, prawns, and lobsters coming from the peeling machines in canning factories. The isolation includes two steps: demineralization with HCl and deproteination with aqueous NaOH [1]. After extraction the chitin is deacetylated to chitosan, and the bio and cellular compatibility of the materials is re-introduced by preparing chitosan composites by conjugation of proteins and peptides of desirable properties. Many of such composite scaffolds (chitosan–collagen [26,27], chitosan–gelatin [28,29], chitosan–silk fibroin [30,31]) have

Download English Version:

<https://daneshyari.com/en/article/2071468>

Download Persian Version:

<https://daneshyari.com/article/2071468>

[Daneshyari.com](https://daneshyari.com)