REVIEW

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A REVIEW: ROASTED BARLEY AS A PHOTOACOUSTIC CONTRAST AGENT

Nishant M. Patel*, Rahul R. Borse, Laxmi A. Premchandani, Amitkumar R. Dhankani, S. P. Pawar

Department of Pharmaceutics, P.S.G.V.P.Mandal's, College of Pharmacy, Shahada-425409, Dist. - Nandurbar, Maharashtra, India.

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ABSTRACT

A contrast agent or contrast medium is a substance used to increase the contrast of structures or fluids within the body in medical imaging. Contrast agents absorb or alter external electromagnetism or ultrasound, which is different from radiopharmaceuticals, which emit radiation themselves. Often, contrast materials allow the radiologist to distinguish normal from abnormal conditions. Contrast materials are not dyes that permanently discolor internal organs. They are substances that temporarily change the way x-rays or other imaging tools interact with the body. Photoacoustic computed tomography (PACT) is an emerging imaging modality. While many contrast agents have been developed for PACT, these typically cannot immediately be used in humans due to the lengthy regulatory process. Contrast agents, in order to be approved for human use, need to go through extensive screening in terms of safety and usability. Researchers bought more than 200 types of tea, chocolate, herbs and other foodstuffs in an attempt to find an edible contrast agent. Roasted barley, a grain used to produce beer, bread and other products, provided the best results. In this article we are reviewing the use of roasted barley as a contrast mediafor imaging swallowing disorders.

KEYWORDS: Photoacoustic computed tomography, barley, contrast agent, barium

Corresponding author: Nishant. M. Patel

E-mail: nishantpatel264@gmail.com

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INTRODUCTION

Contrast materials, also called contrast agents or contrast media, are used to improve pictures of the inside of the body produced by x-rays, computed tomography (CT), magnetic resonance (MR) imaging, and ultrasound that is this is a substance used to increase the contrast of structures or fluids within the body in medical imaging[1]. Often, contrast materials allow the radiologist to distinguish normal from abnormal conditions.

Contrast materials are not dyes that permanently discolor internal organs. They are substances that temporarily change the way x-rays or other imaging tools interact with the body [2].

Contrast agents absorb or alter external electromagnetism or ultrasound, which is different from radiopharmaceuticals, which emit radiation themselves. In x-rays, contrast agents enhance the radio density in a target tissue or structure. In MRI's, contrast agents shorten (or in some instances increase) the relaxation times of nuclei within body tissues in order to alter the contrast in the image. Contrast agents are commonly used to improve the visibility of blood vessels and the gastrointestinal tract. [2]

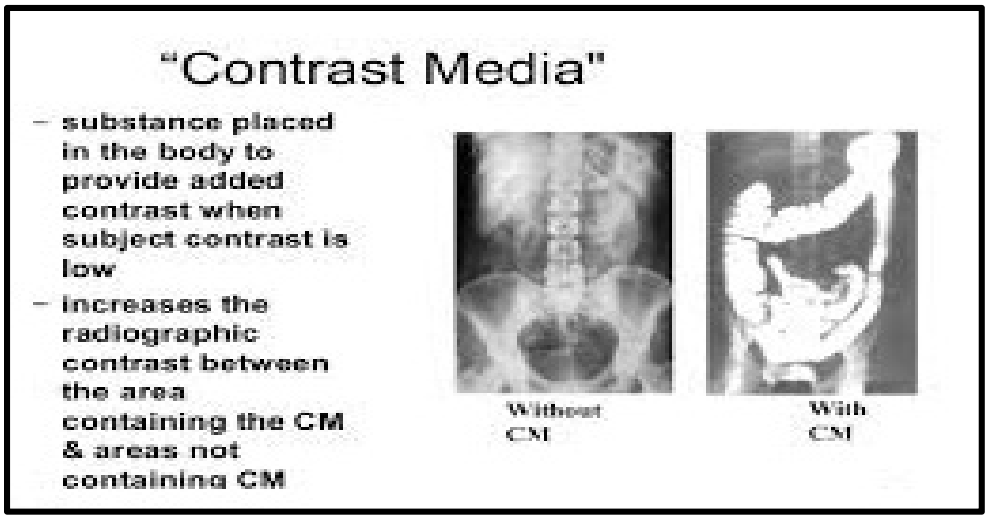

Fig. 1. : Contrast Materials in Imaging Exams

Contrast materials enter the body in one of three ways. They can be: [1]

- Swallowed (taken by mouth or orally)
- Administered by enema (given rectally)
- Injected into a blood vessel (vein or artery; also called given intravenously or intra-arterially)

Following an imaging exam with contrast material, the material is absorbed by the body or eliminate through urine or bowel movements. There are several types of contrast materials [1]:

- Iodine-based and barium-sulfate compounds are used in x-ray and computed tomography (CT) imaging exams. When iodine-based and barium-sulfate contrast materials are present in a specific area of the body, they block or limit the ability of x-rays to pass through. As a result, blood vessels, organs and other body tissue that temporarily

contain iodine-based or barium compounds change their appearance on x-ray or CT images.

- Gadolinium is the key component of the contrast material most often used in magnetic resonance (MR) exams. When this substance is present in the body, it alters the magnetic properties of nearby water molecules, which enhances the quality of MR images.
- Saline (salt water) and gas (such as air) are also used as contrast materials in imaging exams. Micro bubbles and microspheres have been administered for ultrasound imaging exams, particularly exams of the heart.

But these contrast materials carry a risk of causing an allergic reaction or adverse reaction therefore to avoid such problems attempt is made to find natural contrast media.

What are the Side Effects of Radiographic Contrast Media?

The currently used contrast media are based on the chemical modification of a 2, 4, 6-tri-iodinated benzene ring and are indispensable in the practice of radiology, for both diagnostic and therapeutic purposes. Side effects of radiographic contrast media range from a mild inconvenience, such as itching, to a life-threatening emergency and they are as follows[3]:

- **Hypersensitivity Reaction [4]:**

  Mild hypersensitivity reactions (incidence <3%) consist of immediate skin rashes, flushing or urticardia pruritus, rhinorrhea, nausea, brief retching, and/or vomiting,diaphoresis, coughing and dizziness; moderate to severe (incidence <0.04%) reactions include persistent vomiting, diffuse urticardia, headache, facial edema, laryngeal edema, mild bronchospasm or dyspnea, palpitations, tachycardia or bradycardia, abdominal cramps, angioedema, coronary artery spasm, hypertension or hypotension, life-threateningcardiac arrhythmias (i.e. ventricular tachycardia), overt bronchospasm, laryngeal edema, cardiac failure and loss of consciousness, pulmonary edema, seizures, syncopeMortality is less than 1 death per 100000 patients.

- **Contrast-Induced Nephropathy:**

  Iodinated contrast may be toxic to the kidneys, especially when given via the arteries prior to studies such as catheter coronary angiography. Non-ionic contrast agents, which are almost exclusively used in computed tomography studies, have not been shown to cause CIN when given intravenously at doses needed for CT studies[5].

- **Contrast-Induced Thyroid Dysfunction:**

  Iodinated radio contrast can induce overactivity (hyperthyroidism) and under activity (hypothyroidism) of the thyroid gland. The risk of either condition developing after a single examination is 2-3 times that of those who have not undergone a scan with iodinated contrast. Thyroid under activity is mediated by a phenomenon called the Wolff–Chaikoff effect, where iodine suppresses the production of thyroid hormones; this is usually temporary but there is an association with longer-term thyroid under activity. Some other people

show the opposite effect, called Jod-Basedow phenomenon, where the iodine induces overproduction of thyroid hormone; this may be the result of underlying thyroid disease (such as nodules or Graves' disease) or previous iodine deficiency. Children exposed to iodinated contrast during pregnancy may develop hypothyroidism after birth and monitoring of the thyroid function is recommended [6].

- **Other side effects:**

  Other forms of adverse reactions include delayed allergic reactions, anaphylactic reactions, and cutaneous reactions, headache, itching, nausea and vomiting, flushing, confusion, diarrhea, abdominal cramps, swelling of throat, etc.

Which imaging exams use contrast materials?

Oral Contrast Materials

Barium-sulfate contrast materials that are swallowed or administered by mouth (orally) are used to enhance x-ray and CT images of the gastrointestinal (GI) tract, including:

- pharynx
- esophagus
- stomach
- the small intestine
- the large intestine (colon)

In some situations, iodine-based contrast materials are substituted for barium-sulfate contrast materials for oral administration.

Rectal Contrast Materials:

Barium-sulfate contrast materials that are administered by enema (rectally) are used to enhance x-ray and CT images of the lower gastrointestinal (GI) tract (colon and rectum).

In some situations, iodine-based contrast materials are substituted for barium-sulfate contrast materials for rectal administration.

Intravenous Contrast Materials:

Iodine-based and Gadolinium-based:

Iodine-based contrast materials injected into a vein (intravenously) are used to enhance x-ray and CT images. Gadolinium injected into a vein (intravenously) is used to enhance MR images. Typically they are used to enhance the:

- internal organs, including the heart, lungs, liver, adrenal glands, kidneys, pancreas, gallbladder, spleen, uterus, and bladder
- gastrointestinal tract, including the stomach, small intestine and large intestine
- arteries and veins of the body, including vessels in the brain, neck, chest, abdomen, pelvis and legs
- soft tissues of the body, including the muscles, fat and skin
- brain
- breast

Microbubble Contrast Materials:

Microbubble contrast materials are tiny bubbles of an injectable gas held in a supporting shell. They are extremely small-smaller than a red blood cell and have a high degree of "echogenicity", or ability to reflect ultrasound waves. Structures with higher

echogenicity will appear brighter on ultrasound. Once the microbubbles are in the bloodstream, ultrasound technology is able capture differences in echogenicity between the gas in the microbubbles and the surrounding tissues of the body, producing an ultrasound image with increased contrast. The microbubbles dissolve, usually within 10 to 15 minutes, and the gas within them is removed from the body through exhalation. Contrast-enhanced ultrasound with microbubbles is a convenient, relatively inexpensive way to improve visualization of blood flow that does not use radiation. It is a useful option for patients with kidney failure or allergies to MRI and/or computed tomography (CT) contrast material.

Microbubble contrast materials can be targeted or untargeted. Untargeted contrast-enhanced ultrasound the more common method helps diagnose certain diseases by providing evaluation of blood flow in the heart and other organs. In targeted contrast-enhanced ultrasound, specific molecules are bound to the surface of the microbubbles. After injection, the microbubbles attach at tissue sites expressing the molecular target, leading to a local increase in the ultrasonic signal.

Contrast-enhanced ultrasound with microbubbles is used in the assessment of:

- blood perfusion in organs
- thrombosis, such as in myocardial infarction
- abnormalities in the heart
- liver and kidney masses
- inflammatory activity in inflammatory bowel disease
- chemotherapy treatment response

Ideal Requirements of contrast agents:

- The contrast agent must improve the visualization of the area of interest by increasing the absolute CT attenuation difference between the target tissue and surrounding tissue and fluids;
- The imaging media should contain a high mole % of the X-ray attenuating atom per agent thereby reducing the volume and concentrations of contrast media needed for imaging;
- The retention-time of the contrast agent in the tissues should be sufficiently long for completion of a CT scan ;
- The contrast agent must localize the tissue of interest and possess favorable bio distribution and pharmacokinetic profiles;
- The contrast agent should be readily soluble or form stable suspensions at aqueous physiological conditions with low viscosity;
- The contrast agent and its metabolites should be non-toxic; and

  The contrast agent should be cleared from the body in a reasonably short amount of time, usually within 24hrs [7].

NATURAL ORAL CONTRAST AGENT

Various artificial oral contrast agents are proposed with beneficial effects in increasing the accuracy and quality of the images, however there might be some associated adverse effects including toxicity, unpalatable, nausea, vomit, diarrhea, dysentery and not well tolerated by patients especially infants and small children[8].

Natural materials should be food and fruit pulps or

tea, which have not shown the previous mentioned side effects. According to some reports, milk, vegetable oil, Ice-cream, Green tea dilute with Gadolinium-chelate. Blueberry juice is a natural food, which can be used for MRI imaging as a positive oral contrast agent. Some Advantages have been reported regarding the natural types of contrast agents over the artificial agents including better taste and tolerability [8].

ROASTED BARLEY AS CONTRAST MEDIA [9]

A Study showed that roasted barley is a superior contrast agent for imaging swallowing disorders. Because many human diets already include barley, it could be fast-tracked for medical use. It has been grown all over the world for thousands of years, and used to make tea, bread, beer and just now finding another use for it as a contrast agent for medical imaging.

Fig. 2. : - New Use of Barley

When hit with a common laser beam, a roasted version of barley may be an ideal and safe contrast agent for diagnosing swallowing disorders.

An alternative to barium [10]:

Swallowing disorders, also known as dysphagia, can be an indication of a serious medical problem. To test for dysphagia, physicians typically have patients to drink thick, chalky liquid called barium Physicians then use X-rays, MRIs or ultrasounds to look inside the throat. Each technique is limited with respect to safety, high-cost and lack of adequate contrast, respectively.

Photoacoustic computed tomography (PACT) is an emerging alternative. Photoacoustic computed tomography (PACT), also referred to as thermo acoustic tomography (TAT), or optoacoustic tomography (OAT), is a biomedical imaging modality in which a combination of optical and ultrasound techniques are leveraged to acquire images of biological tissue/structures while avoiding the use of ionizing radiation or excising tissue. Tissue is irradiated by a laser beam, causing heating locally in the tissue. The expansion of the tissue creates a broadband ultrasound signal, which is measured at a number of locations outside the tissue. The ultrasound data serve as the input into an image reconstruction algorithm that produces maps of the absorbed optical energy density within the tissue [11].

Like barium, patients drink or are injected with a contrast agent- often newly developed nanoparticles made of metals, polymers and other materials. A

laser strikes the nanoparticles, generating pressure waves that can provide nuanced and real-time views inside the body.

One drawback to contrast-enhanced PACT is the often lengthy and expensive regulatory process for new contrast agents.

That's what led us to search for edible alternatives. Because we've been eating or drinking these products, we know they're safe for most people.An advantage of roasted barleyis that it is an inexpensive and commonly available roast foodstuff that is free of nervous system stimulant activity (i.e. like coffee orates).

The researchers focused on dark foods and beverages because the darker the color, the more the foodstuff will absorb wavelengths from the laser and, theoretically, produce a clearer image. Roasted barley provided the best results. Researchers were able to detect individual particles of it through 3.5 centimeters of chicken breast tissue, as well as through human hands.

In addition to swallowing imaging, researchers say roasted barley could potentially be used to diagnose gastrointestinal tract disorders [10].

CONCLUSION:

Roasted barley represents an edible foodstuff that should be considered for photoacoustic contrast imaging of swallowing and gut processes, with immediate potential for clinical translation. These finding shows that use of roasted barley as safe and comestible PA contrast agent. Roasted barley is widely available in the market and could achieve the same tracking effect as synthetic contrast agent. Roasted barley also enabled the first PA imaging of the human swallowing process with limited background noise. Besides human swallowing imaging, roasted barley may potentially be used for clinical imaging to diagnose GI motility disorders. Research of using roasted barley or other foods as contrast agent should open new avenues for PACT biomedical applications.

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