^{99m}Tc-Methyl diphosphonate

^{99m}Tc-MDP

Arvind Chopra, PhD[1]

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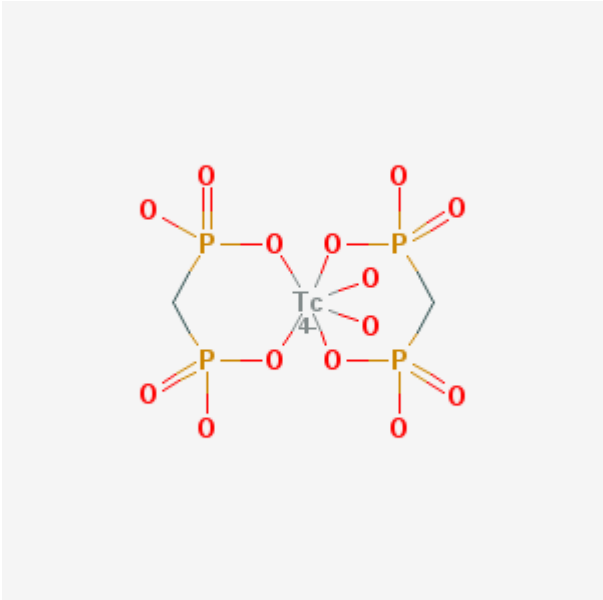
Chemical name:	^{99m}Tc-Methyl diphosphonate
Abbreviated name:	^{99m}Tc -MDP
Synonym:	^{99m}Tc -Methylene diphosphonate, Technetium 99mTc Medronate
Agent Category:	Compound
Target:	Type 2 class of aminoacyl-tRNA synthetases
Target Category:	Enzymes
Method of detection:	Single photon emission computed tomography (SPECT); planar gamma imaging
Source of signal / contrast:	^{99m}Tc
Activation:	No
Studies:	• *In vitro* • Rodents • Non-primate non-rodent mammals



Structure of ^{99m}Tc-MDP. Click on the above structure for additional information in PubChem.

Table continues on next page...

[1] National Center for Biotechnology Information, NLM, NIH, Bethesda, MD 20894; Email: micad@ncbi.nlm.nih.gov.

Table continued from previous page.

	• Non-human primates • Humans	

Background

[PubMed]

Invasive procedures are often necessary to treat internal bone injuries or disorders. Therefore it is important for individuals providing treatment to accurately diagnose the disorder to provide the most suitable therapy before subjecting the patient to any invasive procedures. Bone injuries are often investigated either by magnetic resonance imaging (MRI) or single-photon emission computed tomography (SPECT) scans using radionuclides (1). The SPECT technique is based on imaging of radionuclides and the fact that certain elements or compounds concentrate selectively in specific tissue. Compared to other imaging techniques, e.g., planar scintigraphy, SPECT provides detailed information about the anatomy and physiological state of the bone (1, 2). Bone SPECT has been used to detect early osteonecrosis of the femoral head in renal transplant patients (3), to investigate internal derangement and stress fractures of the knee (4, 5) and also to monitor bone metastasis in breast (6), gastric (7), and prostate (8) cancers. Imaging with ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP) is the initial method of choice to detect skeletal metastases in cancer patients (9).

For SPECT of the bone, metastable technetium (^{99m}Tc) is tagged onto a phosphonate compound such as MDP to generate ^{99m}Tc-MDP, which selectively concentrates in the bone. Although accumulation of ^{99m}Tc-MDP in the bone is caused by its chemical adsorption onto, and into, the crystalline structure of hydroxyapatite (10), but the enzyme aminoacyl-tRNA synthetase is believed to convert it into ATP analogues that inhibit any ATP-dependent enzymes and result in cellular apoptosis (11). For scintigraphy the labeled compound is administered intravenously to the patient and SPECT is subsequently performed after suitable time periods.

^{99m}Tc-MDP has been approved by the US Food and Drug Administration as an imaging agent to investigate osteogenesis and is commercially available in kit form (12).Results obtained with any new radiolabeled compound being evaluated for bone imaging in clinical trials are compared to those obtained with ^{99m}Tc-MDP.

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Other sources of information:

Protein and mRNA sequence of rat aminoacyl-tRNA synthetase

Gene information regarding rat aminoacyl-tRNA synthetase (GeneID: 114632) (Source: Entrez Gene)

Aminoacyl tRNA synthetase in Online Mendelian Inheritance in Man (OMIM)

Structure of human cytosolic phenylalanyl-tRNA synthase (Source: NCBI)

Synthesis

[PubMed]

Because synthesis of ^{99m}Tc-MDP can be performed at room temperature, a kit for its preparation immediately before use is commercially available (12). The kit includes a vial containing a lyophilized, sterile, nonpyrogenic, and nonradioactive mixture of medronic acid, stannous chloride dehydrate, and p-aminobenzoic acid that is packed under nitrogen. Prior to lyophilization, pH of the mixture is adjusted to between 6.5 and 7.5 with hydrochloric acid or sodium hydroxide. To prepare ^{99m}Tc-MDP, sodium pertechnetate (^{99m}Tc), available as a sterile nonpyrogenic preparation from commercial sources, is injected into the vial containing the lyophilized mixture. To mix the solution, the vial is swirled gently until the contents are completely dissolved. According to the manufacturer, the labeling is rapid and quantitative. The maximum recommended amount of ^{99m}Tc to add to the vial is 500 mCi (18.5 GBq). The product information and insert can be viewed at the manufacturers website.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The mechanism of ^{99m}Tc-MDP accumulation in bone was investigated in mice calvaria, osteoblast-like cells, collagen sponges, and hydroxyapatite powder (10). Uptake of the label was observed only in cells growing out from the calvaria fragments and in calvaria fragments fixed with ethanol. Pyrophosphate and EDTA reduced the accumulation of ^{99m}Tc-MDP on the calvaria fragments. No correlation was observed between the number of osteoblast-like cells and the accumulation of ^{99m}Tc-MDP. No accumulation of ^{99m}Tc-MDP was seen in the collagen sponges. These observations suggest that ^{99m}Tc-MDP accumulates on the bone by chemical adsorption and incorporation into the hydroxyapatite structure.

The uptake of ^{99m}Tc-MDP was investigated in two rat tibial bone models (13). In one model, the bone had a specific injury, and in the other there was osteomyelitis. Both models were evaluated by scintigraphy and ^{31}P magnetic resonance spectroscopy for pH, mineral phosphate/creatinine phosphate ratio (Pi/PCr), and ATP/PCr ratio over a three-week period. In both models the ^{99m}Tc-MDP uptake peaked at ~one week and gradually

decreased thereafter. With the scintigram the injured bone demonstrated distinct uptake, but there was a diffused uptake in the osteomyelitis model. Only the osteomyelitis model showed a significant change in pH and ATP/PCr, but not Pi/Cr. This indicated that the accumulation of ^{99m}Tc-MDP in the bone was affected by the disease type and environmental factors such as pH and phosphate concentration.

Animal Studies

Rodents

[PubMed]

The uptake of ^{99m}Tc-MDP and ^{32}P incorporation was used as a measure of bone healing during endosteal healing with titanium, hydroxyapatite (these are considered bone-bonding materials), or stainless steel (does not bind to bone) implants in rat tibial bone after bone marrow ablation (14). The distribution of ^{99m}Tc-MDP and ^{32}P was observed to vary according to the implant, which indicated that the implants influenced bone healing. The investigators suggest that the distribution and uptake of the two labels may be useful parameters to study bone bonding.

The effect of mitomycin-C, a drug used to treat cancer, on the biodistribution of ^{99m}Tc-MDP in mice was investigated (15). Although the drug affected radioactivity uptake in the stomach, ovary, pancreas, uterus, kidneys, spleen, thymus, heart, liver, and lungs, no significant change was observed in thyroid, brain, or bones of the animals. The investigators concluded that mitomycin-C did not interfere with ^{99m}Tc-MDP bone SPECT; however, because it changed the uptake in some organs, any hot spots should be examined carefully for diagnosis.

The whole-body (WB) retention of ^{47}CaCl and ^{99m}Tc-MDP was investigated in three bone disease models (osteomalacic, steroid-induced osteoporosis, and osteoporosis) in rats (16). The three disease models showed marked differences in WB retention of the two radiopharmaceuticals after 24 h of administration. On the basis of these observations, the investigators suggest that these radiopharmaceuticals can be used to differentiate the various bone diseases prior to detection of radiological changes in the animal models.

Other Non-Primate Mammals

[PubMed]

Drost et al. (17) investigated the use of ^{99m}Tc-MDP scintigraphy to determine the onset time frame, distribution, and appearance of bone lesions in dogs infected with *Hepatozoon americanum* oocytes. These protozoans proliferate on the long bones, pelvis, vertebrae, and skull of the animals. The investigators described the appearance of the lesions and concluded that scintigraphy can be used to evaluate the *H. americanum* lesions in the animals.

Scintigraphy using ^{99m}Tc-MDP was performed on lame dogs after clinical examination; radiography and synovial fluid analysis could not localize the cause of lameness to a specific area of pain (18). After bone scintigraphy, the investigators concluded that the highly sensitive and relatively specific uptake of the label could be used to localize and characterize, or exclude, the skeletal lesions that caused lameness in most dogs examined in this study.

The effect of ^{99m}Tc-MDP and ^{99m}Tc-dicarboxypropane diphosphonate (^{99m}Tc-DPD) on bone scan image quality and time in dogs with osteoarthritis was evaluated (19). The investigators observed that both labels yielded similar results for radioactivity uptake and image quality; however, ^{99m}Tc-DPD was more efficient than ^{99m}Tc-MDP in reducing the overall time of scintigraphy.

Some SPECT work has also been done to diagnose tooth infections (20) and paranasal disorders (21) in horses.

Non-Human Primates

[PubMed]

Scintigraphy with ^{99m}Tc-MDP was used to evaluate the healing of long bone fractures in baboons (22). The investigators concluded that ^{99m}Tc-MDP scintigraphy was an accurate technique to investigate the physiological activity of bones. The same investigators also concluded that this technique was a valuable diagnostic tool in traumatic orthopedic surgery for the quantitative and qualitative evaluation of long bone healing in these animals (23).

Human Studies

[PubMed]

Several investigators have shown that ^{99m}Tc-MDP scans (WB bone or specific body parts) can be used to monitor, diagnose, and detect a variety of human diseases (24-27).

A retrospective study assessed the use of WB bone scintigraphy (WB BSc) with ^{99m}Tc-MDP to monitor the effect of biphosphonate treatment in patients with breast cancer and bone metastasis (6). After compiling the results the investigators concluded that WB BSc with ^{99m}Tc-MDP was a reliable method to assess this therapy in the treatment planning of breast cancer patients. Binnie et al. have suggested the use of pre-therapeutic ^{99m}Tc-MDP bone scans to plan targeted radionulide therapy for bone metastases caused by prostate cancer (28). On the other hand, it has been suggested that ^{18}F-fluoride positron emission tomography/computed tomography is a more sensitive and specific method than ^{99m}Tc-MDP planar scintigraphy to detect bone metastases in prostate cancer patients (8). The use of bone scintigraphy in common osteolytic tumors has been discussed and illustrated by Wang et al. (29).

A WB BSc with ^{99m}Tc-MDP of a man with medullary carcinoma of the thyroid revealed hepatic metastases that were later confirmed with a computed tomography scan (24), which indicated that WB BSc with ^{99m}Tc-MDP can be used to detect hepatic metastasis. In another study, WB BSc with ^{99m}Tc-MDP revealed an unusually extensive metastatic disease in the abdominal region, without lung involvement, in a patient who underwent intensive chemotherapy (25). The investigators recommend that patients with osteosarcoma who have signs of intestinal or abdominal obstruction should be subject to bone scintigraphy to reveal any unexpected metastatic foci.

^{99m}Tc-MDP scintigraphy has also been used to detect femoral head avascular osteonecrosis (26) and the characteristic lesions of Erdheim-Chester disease (27).

Supplemental Information

[Disclaimer]

No information is currently available.

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