thinking corresponds to the notion that a higher iodine concentration may provide better diagnosis. The development of non-ionic monomeric contrast agents and in particular non-ionic bis(triiodophenyl) dimers such as iodixanol (EP 108638) has provided contrast media with reduced osmotoxicity. This has allowed contrast with effective iodine concentration to be achieved with hypotonic solution, and has even allowed correction of ionic imbalance by inclusion of plasma ions while still maintaining the contrast medium at the desired osmolality, e.g.as for Visipaque™.

However, to reduce the risk of adverse events, especially in susceptible subjects, to improve patient safety and to reduce costs, there is now a desire to reduce the amount (volume and iodine dose) of X-ray contrast media administered to patients undergoing X-ray examinations.

WO 2009/008734 of GE Healthcare AS discloses a new class of compounds and their use as X-ray contrast agents. The compounds are dimers containing two linked iodinated phenyl groups. The bridge linking the two iodinated phenyl groups is a straight C3 to C8 alkylene chain optionally substituted by one to six –OH or OCH3 groups. A range of compounds are covered by the general formula (I) of the application and many specific compounds are suggested. Compound I, which is one specific dimeric X-ray contrast agent, falling within the formula I of WO2009/008734, given the International Non-proprietary name loforminol, has been found by the applicant to have particularly favourable properties. Compound I is 5,5'-((2-hydroxypropane-1,3-diyl)bis(formylazanediyl))bis(N1,N3-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide).

Summary:

The applicant has now surprisingly identified a new X-ray diagnostic composition providing improved patient safety. The new composition which is useful as a contrast media in X-ray imaging comprises loforminol as the contrast agent, and provides a low concentration of iodine. A composition has been identified providing an optimised amount of salts.

Hence, ~~in a first aspect~~ the disclosure provides an X-ray composition comprising loforminol and a pharmaceutically acceptable carrier or excipient, wherein the composition comprises an iodine concentration of 10-200 mg I/ml and a sodium ion

concentration of 70 -120 mM. The iodine present in the composition is mainly from Ioforminol, which includes six iodine atoms per molecule.

In a first aspect, there is provided an X-ray composition comprising Ioforminol and a pharmaceutically acceptable carrier or excipient, wherein the composition comprises an iodine concentration of 10-200 mg I/ml and a sodium ion concentration of 70-120 mM and a calcium ion centration of 0.5-1.3mM.

~~In a second aspect, there is provided a composition as described above for use in a method of x-ray examination comprising~~

~~applying an X-ray radiation dose to a body that had been administered with the composition,~~

~~examining the body with a diagnostic device and~~

~~compiling data from the examination.~~

In a second~~third~~ aspect, there is provided a method of X-ray examination, comprising applying an X-ray radiation dose to a body that had been administered with a composition as disclosed above~~comprising Ioforminol and a pharmaceutically acceptable carrier or excipient wherein the composition comprises an iodine concentration of 10-200 mg I/ml and a sodium ion concentration of 70-120 mM~~,

examining the body with a diagnostic device and

compiling data from the examination.

Brief description of the drawings:

The Figures 1 to 6 show iodine contrast enhancement by measuring the mean X-ray attenuation values within circular region of interests, using compositions of Ioforminol of different concentrations, at different tube voltage energies and using different software to reduce noise. For the Figures 1 to 3 the region of interest is the aorta, and for the Figures 4-6 the region of interest is the liver.

Figure 1 shows images using Ioforminol of 320 mg I/ml and 200 mg I/ml, and tube voltage energies of 120 and 80 KVp.

Figure 2 shows images using Ioforminol of 320 mg I/ml and 160 mg I/ml, and tube voltage energies of 120 and 80 KVp.

Figure 3 shows images using Ioforminol of 320 mg I/ml and 200 mg I/ml, and tube voltage energies of 120 and 100 KVp.

Figure 4 shows images using Ioforminol of 320 mg I/ml and 200 mg I/ml, and tube voltage energies of 120 and 80 KVp.

Claims

1. An X-ray composition comprising Ioforminol and a pharmaceutically acceptable carrier or excipient, wherein the composition comprises an iodine concentration of 10-200 mg I/ml and a sodium ion concentration of 70-120 mM and a calcium ion centration of 0.5-1.3mM.

~~2. A composition as claimed in claim 1 further comprising a calcium ion concentration of 0.5-1.3 mM.~~

~~3.~~2. A composition as claimed in claim 1 ~~or 2~~ further comprising potassium and/or magnesium ions.

~~4.~~3. A composition as claimed in ~~any of the claims 1 to 4~~claim 1 or 3 wherein the total volume for administration to a body is between 1 and 250 ml.

~~5.~~4. A composition as claimed in ~~any of the claims 1 to 4~~claims 1, 3, or 4 wherein the iodine concentration is about 160 mg I/ml, the sodium concentration about 82 mM and a calcium concentration of 0.7 mM.

~~6.~~5. A composition as claimed ~~in any of the claims 1 to 4~~claims 1, 3, or 4 wherein the iodine concentration is about 200 Mg I/ml, the sodium concentration about 73 mM and a calcium concentration of 0.6 mM.

~~7. Composition as claimed in any of the claims 1 to 6 for use in a method of x-ray examination comprising~~

~~applying an X-ray radiation dose to a body that had been administered with the composition,~~

~~examining the body with a diagnostic device and~~

~~compiling data from the examination.~~

~~8.~~6. A method of X-ray examination, comprising

applying an X-ray radiation dose to a body that had been administered with a composition~~ as claimed in any of the claims 1 to 5comprising loforminol and a pharmaceutically acceptable carrier or excipient wherein the composition comprises an iodine concentration of 10-200 mg I/ml and a sodium ion concentration of 70-120 mM~~,

examining the body with a diagnostic device and

compiling data from the examination.

~~9.~~7. A method as claimed in claim ~~8~~6 enhancing the contrast effect of the loforminol, wherein said dose of radiation has an average energy spectrum substantially corresponding to the k-edge of iodine.

~~10.~~8. A method as claimed in any of the claims 6~~8~~ and 7~~9~~ wherein the X-ray radiation dose is provided by a tube voltage energy in the range of 70-140 kVp.

~~11.~~9. A method as claimed in any of the claims 5~~7~~ to 7~~9~~ wherein the X-ray radiation dose is provided by a tube current in the range of 5-1000 mA.

~~12.~~10. A method as claimed in any of the claims 5~~7~~ to ~~8~~10 further including a step of noise reduction through an advanced image reconstruction method.

~~13.~~11. A method as claimed in claim 9~~11~~ wherein the noise reduction is selected from the iterative image reconstruction methods ASiR and MBIR.

~~14.~~12. A method as claimed in any of the claims 5~~7~~ to 10~~12~~ including Dual Energy CT.