IODINATED CONTRAST MEDIA

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INTRODUCTION

Due to their favorable X-ray attenuation and chemical stability, iodinated contrast media play a crucial role in diagnostic imaging. Their development has progressed along with advances in radiological diagnostic methods and continuous improvements in their safety profile.

CHEMICAL STRUCTURE & CLASSIFICATION

The chemical structure of iodinated contrast media is based on 2,4,6-triiodobenzoic acid, in which three iodine atoms are bonded to a benzene ring. The high atomic number of iodine enables efficient X-ray attenuation, while binding to an organic backbone reduces the toxicity of free iodine. These molecules are water-soluble and are primarily eliminated unmetabolized through the kidneys.

Iodinated compounds used as contrast agents can form monomeric or dimeric structures. Monomers contain a single triiodinated benzene ring, while dimers are composed of two such rings linked together and attached to an additional functional group.

In practice, contrast agents are commonly classified into three groups based on electrical charge and osmolality: ionic (high-osmolar), non-ionic low-osmolar, and non-ionic iso-osmolar compounds. Although non-ionic low-osmolality agents have significantly lower osmolality than ionic ones, their osmolality remains above that of blood (approximately 310 mOsm/kg). In contrast, non-ionic iso-osmolar contrast media have an osmolality comparable to that of human blood due to their dimeric molecular structure, with iodixanol as a representative example. The clinical use of contrast media is determined by their physicochemical properties. Ionic monomers are associated with high osmolality, which increases the risk of adverse reactions. For these agents, higher iodine concentrations were historically required to achieve adequate X-ray attenuation as a consequence of their formulation limitations. Over recent decades, advances in the formulation of contrast media have significantly improved their safety profile, with a key transition from high-osmolality to low-osmolality and iso-osmolar agents, which are today the most commonly used in clinical practice.

VISCOSITY

Viscosity contributes to the safety profile of contrast media, as increased viscosity has been associated with reduced glomerular filtration. It also slows the flow of contrast agents through the renal tubules and elevates tubular pressure. In addition, high-viscosity contrast media may promote erythrocyte aggregation and impair microcirculation. Viscosity increases with higher concentration and lower temperature in a nonlinear relationship, under physiological conditions.

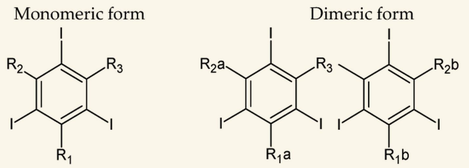


Figure 1: Chemical structure of monomeric and dimeric iodinated contrast media. Adapted from Wrzesińska et al. (2026) [1]

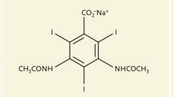
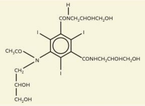
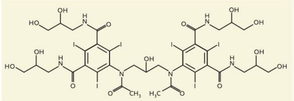
	High Osmolality	Low Osmolality		Iso-osmolality
Molecular Structure				
	Ionic monomer	Ionic dimer	Nonionic monomer	Nonionic dimer
Generic Name (mg contrast/ml)	Diatrizoate meglumine and diatrizoate sodium (760)	Ioxaglate meglumine and ioxaglate sodium (589)	Iopamidol (408) Iopamidol (510) Iopamidol (612) Iopamidol (755)	Iodixanol (550) Iodixanol (652)
Iodine Concentration (mg/ml)	370	320	200–370	270–320
Osmolality (mOsm/kg H_2O)	1551	~600	413–796	290
Viscosity (mPa·sec at 37°C)	10.5	7.5	2.0–9.4	6.3–11.8

Table 1: Characteristics of iodinated contrast media. Adapted from Mehran et al. (2019) [2]

FUTURE OUTLOOK

An ideal contrast agent would combine a high iodine concentration for effective X-ray attenuation with low viscosity and low or iso-osmolality. Since osmolality and viscosity are inversely related in practice, no contrast agent fulfills all ideal criteria. Therefore, the development and selection of contrast media require an optimal balance between physicochemical properties, diagnostic efficacy, and patient safety.

Nanoparticle-based contrast agents are emerging as promising alternatives to iodine-based contrast agents due to improved X-ray attenuation and enhanced image quality, resulting from their high atomic numbers. Their size, together with surface modification, prolongs circulation time in the bloodstream and reduces rapid renal excretion. In addition, they enable targeted imaging, in which the contrast agent selectively accumulates in specific tissues or tumors. Despite these promising properties, further studies are needed to ensure long-term safety, biocompatibility, and efficacy for routine clinical use.

CONCLUSION

Due to their established clinical efficacy and safety, iodinated contrast media remain the gold standard in contrast-enhanced imaging. Despite numerous studies focused on improving current approaches, their clinical implementation remains limited and requires further investigation.

REFERENCES

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