ICG

Indocyanine Green

Diagnostic dye

For determining hepatic function and Liver blood flow
For determining cardiac output and circulatory function
For ophthalmic angiography

DID Indocyanine Green Injection

Distributed by
LDS PHARM CO., LTD

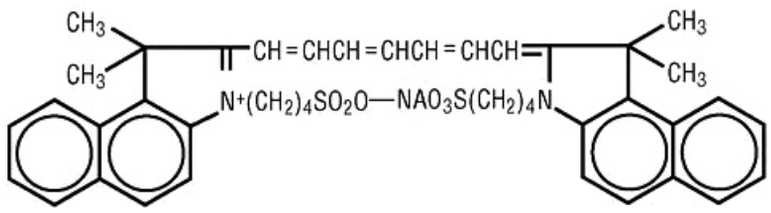
Manufactured by
DONG IN DANG PHARM CO., LTD

Indocyanine Green...

Tricarbocyanine type of dye

: 1H-Benz[e]indolium, 2-[7-[1,3-dihydro-1,1-dimethyl-3-(4-sulfobutyl)-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-3-(4-sulfobutyl)-, hydroxide, inner salt, sodium salt

$C_{43}H_{47}N_2NaO_6S_2$ Molecular Weight 774.96



Solubility : Slightly Soluble in water

Ethanol : slight

Absorbance max : 784nm(MeOH)

Mechanism of Actions and Usage

- Following intravenous injection, Indocyanine Green (ICG) mainly binds to plasma protein and distributed uniformly in the blood within 2-5 minutes
- ICG is then taken up from the plasma almost exclusively by the liver and later secreted unchanged only into the bile within about 20 minutes .

These unique pharmacokinetic features make ICG useful in determination of hepatic & circulatory function by measuring the percentage retention and disappearance rate of ICG from the blood.

- ICG fluoresces in the near-infrared range at about 800 nm. Thus it has an ability to fluoresce better through pigment, fluid, lipid, and hemorrhage than other conventional dyes, thereby increasing the possibility of detecting abnormalities that may be blocked by an overlying thin, subretinal hemorrhage or exudates.

The retention of ICG in the choroidal circulation, coupled with low permeability and unique operating wavelength, makes ICG angiography ideal for imaging choroidal circulation.

Characteristics

· After intravenous injection, ICG is rapidly bound to plasma proteins and distributed uniformly in the blood within 2 – 5 minutes.

· Without being excreted by the kidney, ICG is secreted into the bile by 97% within about 20 minutes. The plasma concentration of ICG decreases in an exponential manner.

· ICG binds almost completely (98%) to plasma proteins and becomes confined to the vascular system. So excessive dye extravasation does not take place in the highly fenestrated choroidal vasculature.

· ICG is not metabolized in the body.

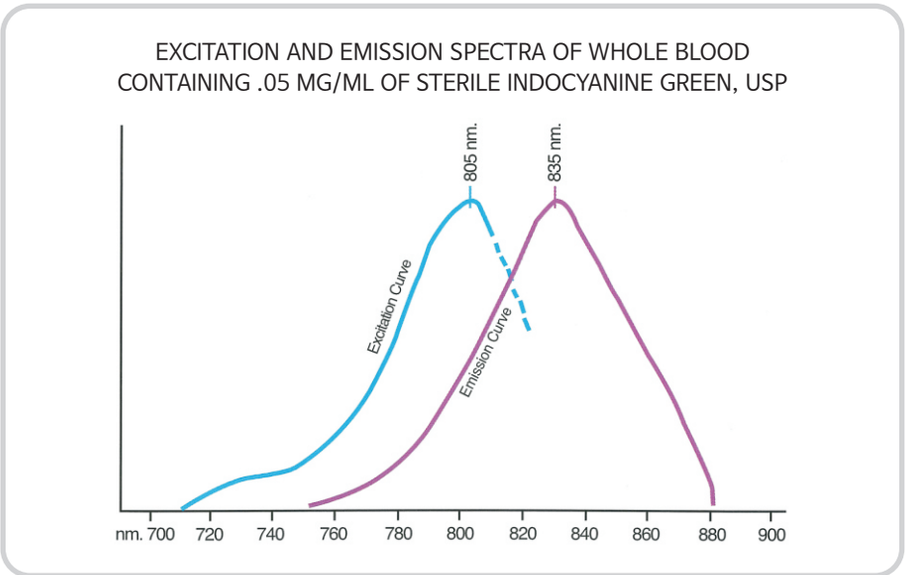
· ICG is rapidly excreted from the body without undergoing enterohepatic circulation.

· Safe dye with slight side effects.

The Excitation and Emission spectra of Indocyanine Green

· The excitation and emission spectra and the absorption spectra of ICG make it useful in ophthalmic angiography.

· The peak absorption and emission of ICG lie in a region (800–850 nm) where transmission of energy by the pigment epithelium is more efficient than in the region of visible light energy.



Liver function test

▶ICG is useful to assess perioperative liver function in hepatectomy.

Assessing liver funtion before hepatectomy by ICG test

Relationship between ICG retenion rate and extent of liver resection

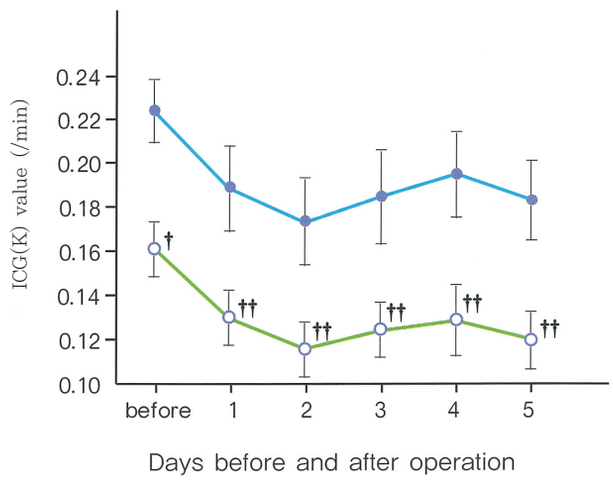
Retention rate	Extent of liver resection
Up to 6%	Without limitation of the extent of liver resection
7 - 15%	Bisegmentectomy at the most
16 - 20%	Segmentectomy
21 - 30%	Superficial liver excision

Bratisl Lek Listy 2001:115-116

Assessing liver function after hepatectomy by ICG test

- There was a significant drop in ICG(K) value, signifying ICG elimination rate constant.
- The ICG(K) values were significantly lower in patients with than without cirrhosis.
- The profiles of postoperative changes in both patients greatly resembled one another
- The estimated ICG(K) value was useful in predicting the postoperative morbidity.

Changes in ICG(K) values after hepatectomy

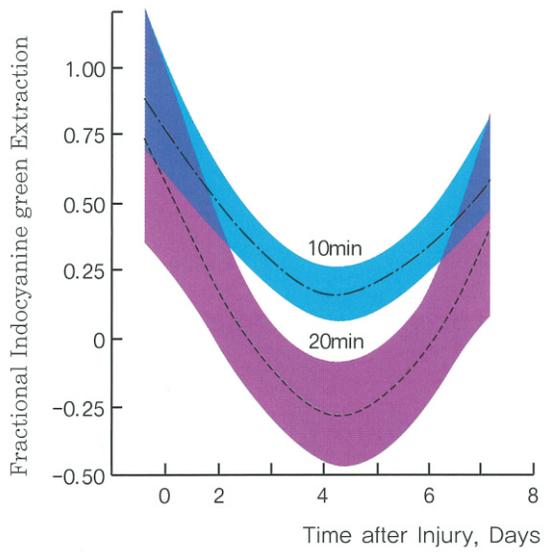


○ Patients with cirrhosis
● Patients without cirrhosis
† $p<0.01$
†† $p<0.05$ by Mann-whitney u test

J Sur Res 2002

The kinetics of Indocyanine Green clearance

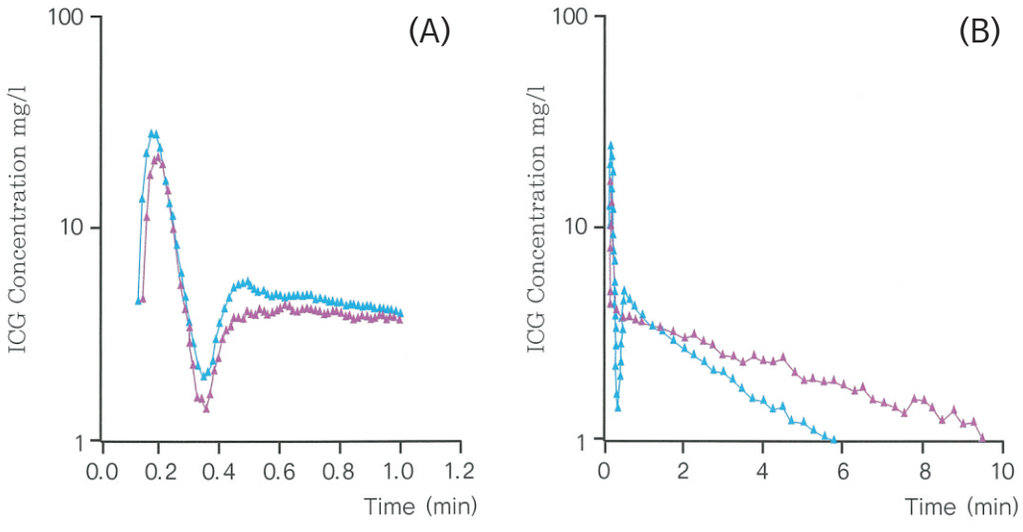
▶ICG clearance was found to be an early indicator of hepatic dysfunction following injury.



Arch surg 1984

Liver function in living liver donor

▶ICG test is able to derive estimate of liver function before and after hepatectomy in living liver donors.



Arterial blood ICG concentration histories for (A) 1 minute and (B) 10 minutes after rapid venous injection in one living liver donor preresection (solid line, symbols) and postresection (dash line, open symbols). ICG expressed as log concentration.

Liver transplantation 2002

Indocyanine Green Angiography

ICG in Angiography for detecting CNV of Exudative AMD

▶ICG was found to be a more useful dye than fluorescein in detecting choroidal neovascularization (CNV) in patients with exudative age-related macular degeneration (AMD).

ICG 12.5 - 25 mg vs fluorescein in detection of CNV

	Detected	Not detected	Rate of detection (%)
ICG 12.5 mg	28	11	28/39 (71.8%)
ICG 25 mg	38	1	38/39 (97.4%)
Fluorescein 500 mg	12	27	12/39 (30.8%)

J Jpn Opthalmol Soc. 2002

▶A dose of 25 mg of ICG was more effective than 12.5 mg in detecting CNV of exudative AMD

Rate of detection depending on the dosage of ICG

Ease of Detection	12.5 mg	25 mg
Very easy	7	9
Easy	14	22
Slightly difficult	7	7
Difficult	11	1
Detection rate	21/39 (53.8%)	21/39 (79.5%)

J Jpn Opthalmol Soc. 2002

Indocyanine Green Angiography

Utility of ICG guided Laser photocoagulation of CNV in Age-related Mascular Degeneration

▶ICG angiography was equivalent to fluorescein angiography in utility of photocoagulation of CNV in AMD.

The sucess rate of photocoagulation

Indocyanine Green Angiography	Fluorescein Angiography	P-Value
81%	82%	0.84

J Jpn Opthalmol Soc. 2002

▶There was no statistically significant difference between the ICG angiography (IA) group and fluorescein angiography (FA) group in the success rate of laser photocoagulation for the following lesions.

Lesions	IA group	FA group	P-Value
Retinal detachment	84%	89%	0.51
Serous pigment epithelial detachment	72%	64%	0.71
Hemorrhagic pigment epithelial detachment	82%	75%	0.52
Others	90%	88%	0.81

J Jpn Opthalmol Soc. 2002

ICG Indocyanine Green

Rx only / Sterile
Pharmacologic class : 728

Drug Information

Composition	1 Vial contains Active ingredient : indocyanine green (USP) ---------- 25.0 mg * Aqueous Solvent : Water for injection (KP) ------- 20.0 mL / plastic vial
Description	Sterile lyophilized dark bluish-green powder in a colorless clear vial to be dissolved with Aqueous Solvent provided before use
Indications and Usage	1. Liver function tests (determination of plasma elimination rate, blood retention rate and hepatic blood flow) : Diagnosis of hepatic diseases and assessment of the prognosis 2. Circulatory function tests (determination of cardiac output, mean circulation time and abnormal blood flow) : Diagnosis of cardiovascular diseases 3. Fluorescence ophthalmic angiography
Dosage & Administration	**A. For liver function tests** (1) For determination of plasma elimination and blood retention rates 25mg of DID Indocyanine green Inj.TM powder should be dissolved with 5 nL of the Aqueous Solvent provided for this product to make a 5 mg/mL solution.and then injected intravenously at a dose of 0.5 mg of kg of body weight via the cubital vein within 30 seconds while closely monitoring the patient's condition. (2) For determination of hepatic blood flow 25 mg of DID Indocyanine green Inj.TM should be dissolved with the Aqueous Solvent in a small amount as possible and then diluted with physiological saline to make a 2.5 - 5 mg/mL solution. The amount of solution containing 3 mg of indocyanine green should be injected intravenously and then via drip infusion at a constant rate, 0.27 - 0.49 mg/min for approximately 50 min until completion of blood sampling. **B. For circulatory function tests** Indocyanine green solution is injected into various vessels from the heart chambers to the peripheral veins generally via the antebrachial vein. The usual adult dose of DID Indocyanine green Inj.TM may be adjusted to an amount containing 5 - 10 mg of indocyanine green. **C. For fluorescence ophthalmic angiography** Dosages up to 40 mg Indocyanine green dye in 2 mL of aqueous solvent have been found to give optimal angiograms, depending on the imaging equipment and technique used. The antecubital vein injected Indocyanine green dye bolus should immediately be followed by a 5 mL bolus of normal saline.
Precautions	ICG is unstable in aqueous solution and must be used within 6 hours after reconstitution. For more information, see package insert.
Storage	Light resistant, hermetic container. Store at room temperature (1 - 30 ℃)

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