obstruction of cardiac ejection, such as idiopathic hypertrophic subaortic stenosis. It should also be used with caution in patients with acute myocardial infarction, and in cardiogenic shock complicated by severe hypotension. Hypovolaemia should be corrected before treatment.

Interference with diagnostic tests. Contamination of blood samples with dobutamine has been reported to produce falsely decreased creatinine values in an enzymatic test.[1] Colorimetric measurements of creatinine were not affected.

1. Daly TM, *et al.* "Bouncing" creatinine levels. *N Engl J Med* 1996; **334:** 1749–50.

Interactions

As for Sympathomimetics, p.1407. Most interactions with dobutamine are due to its direct $beta_1$ agonist effects on the heart, but use with beta blockers may allow its alpha- and $beta_2$-agonist effects to become apparent.

Pharmacokinetics

Like adrenaline (p.1204), dobutamine is inactive when given orally, and it is rapidly inactivated in the body by similar processes. It has a half-life of about 2 minutes. Conjugates of dobutamine and its major metabolite 3-*O*-methyldobutamine are excreted primarily in urine, with small amounts eliminated in the faeces.

◊ The primary mechanism of clearance of dobutamine appears to be distribution to other tissues, and not metabolism or elimination. It has a half-life of about 2 minutes and plasma concentrations of dobutamine reach steady state about 10 to 12 minutes after the start of an infusion. Dobutamine is used mainly for the short-term treatment of heart failure and any pharmacokinetic changes in this condition have no clinical implications in dosage titration.[1]

The pharmacokinetics of dobutamine and other cardiovascular drugs in children have been reviewed.[2]

1. Shammas FV, Dickstein K. Clinical pharmacokinetics in heart failure: an updated review. *Clin Pharmacokinet* 1988; **15:** 94–113.
2. Steinberg C, Notterman DA. Pharmacokinetics of cardiovascular drugs in children: inotropes and vasopressors. *Clin Pharmacokinet* 1994; **27:** 345–67.

Uses and Administration

Dobutamine is a sympathomimetic (p.1408) with direct effects on $beta_1$-adrenergic receptors, giving it a prominent inotropic action on the heart. It also has some alpha- and $beta_2$-agonist properties. Although it is structurally related to dopamine (p.1273), it has no specific dopaminergic properties; however, like dopamine, the inotropic action of dobutamine on the heart is associated with less cardiac-accelerating effect than that of isoprenaline.

Dobutamine is used to increase the contractility of the heart in acute heart failure, as occurs in cardiogenic shock (p.1183) and myocardial infarction (p.1175); it is also used in septic shock. Other circumstances in which its inotropic activity may be useful are during cardiac surgery and positive end-expiratory pressure ventilation.

Dobutamine is used as the hydrochloride but doses are expressed in terms of the base; 1.12 micrograms of the hydrochloride is equivalent to about 1 microgram of base. It is given by intravenous infusion as a dilute solution (0.25 to 5 mg/mL), in glucose 5% or sodium chloride 0.9%; other fluids may also be suitable and the manufacturers' guidelines should be consulted.

In the management of **acute heart failure**, dobutamine is given at a usual rate of 2.5 to 10 micrograms/kg per minute, according to the patient's heart rate, blood pressure, cardiac output, and urine output. A range of 0.5 up to 40 micrograms/kg per minute has occasionally been required. It has been recommended that treatment with dobutamine should be discontinued gradually.

Dobutamine is also used as an alternative to exercise in **cardiac stress testing**. A solution containing 1 mg/mL is given via an infusion pump in a dose of 5 micrograms/kg per minute for 8 minutes. The dose is then increased by increments of 5 micrograms/kg per minute up to a usual maximum of 20 micrograms/kg per minute, with each dose being infused for 8 minutes before the next increase; doses of up to 40 micrograms/kg per minute have sometimes been used. The ECG should be monitored continuously and the infusion stopped if arrhythmias, marked ST segment depression, or other adverse effects occur.

Action. Although dobutamine is usually considered to be a $beta_1$ agonist, *animal* studies suggest that its ability to stimulate $alpha_1$- and $beta_2$-adrenergic receptors may be as great as its $beta_1$-stimulant properties. It has been proposed that the inotropic action results from a combination of alpha-stimulant activity on myocardial $alpha_1$ receptors, a property residing mainly in the (–)-enantiomer, with $beta_1$ stimulation by the (+)-enantiomer; peripherally, alpha-mediated vasoconstriction would be opposed by the $beta_2$-agonist properties of the (+)-enantiomer, resulting in the net inotropic action with relatively little effect on blood pressure seen with the racemic mixture used clinically.[1]

Dobutamine has a thermogenic effect,[2] increasing oxygen delivery and utilisation in healthy individuals. However, using it for this purpose in critically ill patients did not improve patient outcome and in some cases might have been harmful.[3]

1. Ruffolo RR. The mechanism of action of dobutamine. *Ann Intern Med* 1984; **100:** 313–14.
2. Bhatt SB, *et al.* Effect of dobutamine on oxygen supply and uptake in healthy volunteers. *Br J Anaesth* 1992; **69:** 298–303.
3. Hayes MA, *et al.* Elevation of systemic oxygen delivery in the treatment of critically ill patients. *N Engl J Med* 1994; **330:** 1717–22.

Administration in children. Dobutamine and dopamine are both used for inotropic support in children. A study[1] in children undergoing cardiac surgery suggested that dobutamine may be preferred to dopamine since the latter could cause pulmonary vasoconstriction (see under Precautions for Dopamine, p.1273). In preterm infants, one study[2] reported that dobutamine may have a greater effect on systemic blood flow than dopamine, but a systematic review[3] found that dopamine was more effective than dobutamine in the short-term treatment of hypotension although there was insufficient evidence of long-term benefit or safety with either drug for firm recommendations to be made.

1. Booker PD, *et al.* Comparison of the haemodynamic effects of dopamine and dobutamine in young children undergoing cardiac surgery. *Br J Anaesth* 1995; **74:** 419–23.
2. Osborn D, *et al.* Randomized trial of dobutamine versus dopamine in preterm infants with low systemic blood flow. *J Pediatr* 2002; **140:** 183–91.
3. Subhedar NV, Shaw NJ. Dopamine versus dobutamine for hypotensive preterm infants. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2003 (accessed 07/10/05).

Diagnosis and testing. Dynamic exercise is the established mode of stress for the assessment of cardiac function. In patients who are unable to exercise, a dobutamine infusion is one of the best alternative ways of producing a pharmacological stress.[1,2] It is widely used as an adjunct in echocardiography, often combined with atropine, and may give better sensitivity than adenosine or dipyridamole;[1,3] it may also have a role with other imaging techniques such as magnetic resonance imaging.[4] However there have been instances of severe cardiovascular complications attributable to dobutamine.[5]

1. Cheitlin MD, *et al.* ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). Summary article: *Circulation* 2003; **108:** 1146–62. Full text: http://www.americanheart.org/downloadable/heart/1060182581039Echocleanfulltext.pdf (accessed 07/10/05)
2. Marwick TH. Stress echocardiography. *Heart* 2003; **89:** 113–18.
3. Martin TW, *et al.* Comparison of adenosine, dipyridamole, and dobutamine in stress echocardiography. *Ann Intern Med* 1992; **116:** 190–6.
4. Paetsch I, *et al.* Comparison of dobutamine stress magnetic resonance, adenosine stress magnetic resonance, and adenosine stress magnetic resonance perfusion. *Circulation* 2004; **110:** 835–42.
5. Lattanzi F, *et al.* Dobutamine stress echocardiography: safety in diagnosing coronary artery disease. *Drug Safety* 2000; **22:** 251–62.

Heart failure. Dobutamine may be used in the management of acute heart failure, including decompensated chronic heart failure (see Cardiogenic Shock, under Shock, p.1183). It may also have a role in patients with severe chronic heart failure (p.1165), either as a bridge to transplantation or for palliative therapy. In less severe cases, intermittent infusions of dobutamine have been tried. A study[1] using pulsed therapy with dobutamine (30 minutes daily for 4 days each week for 3 weeks) reported symptomatic improvements similar to those achieved with exercise, but another study[2] using intermittent therapy (24 hours every 2 to 3 weeks for 6 months) failed to show any benefit. There have also been reports of sudden death in patients receiving dobutamine as infusions for 48 hours per week, and another study[3] was halted for this reason. Long-term use of intermittent dobutamine is therefore not generally recommended.[4]

1. Adamopoulos S, *et al.* Effects of pulsed β-stimulant therapy on β-adrenoceptors and chronotropic responsiveness in chronic heart failure. *Lancet* 1995; **345:** 344–9.
2. Elis A, *et al.* Intermittent dobutamine treatment in patients with chronic refractory congestive heart failure: a randomized, double-blind, placebo-controlled study. *Clin Pharmacol Ther* 1998; **63:** 682–5.
3. Dies F, *et al.* Intermittent dobutamine in ambulatory outpatients with chronic cardiac failure. *Circulation* 1986; **74:** (suppl II): 38.
4. Hunt SA, *et al.* ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). Summary article: *J Am Coll Cardiol* 2005; **46:** 1116–43. Full version: http://content.onlinejacc.org/cgi/reprint/46/6/e1.pdf (accessed 19/08/08)

Preparations

BP 2008: Dobutamine Intravenous Infusion;
USP 31: Dobutamine for Injection; Dobutamine in Dextrose Injection; Dobutamine Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Dobucard; Dobuject†; Dobutrex†; Duvig; ***Austral.:*** Dobutrex; ***Austria:*** Inotop; ***Belg.:*** Dobutrex†; Dobutrexmerck; ***Braz.:*** Biodobutin†; Dobtan; Dobutabbott; Dobutal†; Dobutil†; Dobuton; Dobutrex†; Neobutamina; ***Canad.:*** Dobutrex†; ***Chile:*** Bagobutam†; Dobutrex†; ***Cz.:*** Dobuject; Dobutrex; ***Denm.:*** Dobutrex†; ***Fin.:*** Dobuject; Dobutrex†; ***Fr.:*** Dobutrex†; ***Gr.:*** Dobutan; Inotrex; ***Hong Kong:*** Dobutrex†; ***Hung.:*** Dobutrex†; ***India:*** Dobutrex; ***Indon.:*** Cardiject; Dobuject; Dobutel; Inotrop; ***Irl.:*** Dobutrex†; Posiject†; ***Israel:*** Butamine; Dobuject; Dobutam†; ***Ital.:*** Dobutrex†; Miozac; ***Jpn:*** Dobupum; ***Malaysia:*** Dobucard†; Dobutrex†; ***Mex.:*** Cryobutol; Dobuject; Dobutrex; Kardion†; Oxiken; ***Norw.:*** Dobutrex†; ***NZ:*** Dobutrex†; ***Philipp.:*** Dobuject; Dobutrex; ***Pol.:*** Dobuject; ***Port.:*** Dobucor; Dobutina; Inotrex; ***S.Afr.:*** Cardiject; Dobutrex; Posiject†; ***Singapore:*** Dobuject†; ***Spain:*** Dobucor; Dobutrex†; ***Swed.:*** Dobutrex; ***Switz.:*** Dobutrex; ***Thai.:*** Cardiject; Dobuject; Dobutrex†; ***UK:*** Dobutrex†; Posiject†; ***USA:*** Dobutrex†; ***Venez.:*** Doburan; Dobutrex†; Dobuxin.

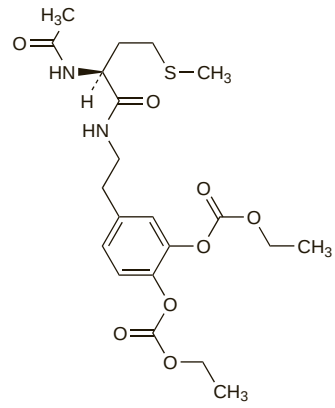
Docarpamine *(rINN)*

Docarpamina; Docarpaminum; TA-870; TA-8704. (–)-(*S*)-2-Acetamido-*N*-(3,4-dihydroxyphenethyl)-4-(methylthio)butyramide bis(ethyl carbonate) ester.

Докарпамин

$C_{21}H_{30}N_2O_8S$ = 470.5.

CAS — 74639-40-0.



Profile

Docarpamine is an orally active prodrug of dopamine (p.1273) that has been used in the treatment of acute heart failure.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Tanadopa†.

Dofetilide *(BAN, USAN, rINN)*

Dofetilid; Dofetilida; Dofétilide; Dofetilidi; Dofetilidum; UK-68798. β-[(*p*-Methanesulfonamidophenethyl)methylamino]methanesulfono-*p*-phenetidide.

Дофетилид

$C_{19}H_{27}N_3O_5S_2$ = 441.6.

CAS — 115256-11-6.

ATC — C01BD04.

ATC Vet — QC01BD04.