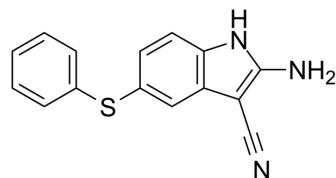


Amphethinile

Cat. No.:	HY-100190
CAS No.:	91531-98-5
Molecular Formula:	C ₁₅ H ₁₁ N ₃ S
Molecular Weight:	265.33
Target:	Microtubule/Tubulin
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Amphethinile is an anti-tubulin agent. The affinity constant for the association (K_a) of Amphethinile with tubulin is 1.3 μ M.
IC₅₀ & Target	K_a : 1.3 μ M (Tubulin) ^[1]
In Vitro	Amphethinile shows a remarkable similarity to colchicine in terms of its binding to tubulin and inhibition of microtubular assembly. Amphethinile binds strongly to microtubule protein ($K_a=1.3 \mu$ M). This interaction has been shown to be capable of inhibiting tubulin assembly, but shows no rapid stimulation of disassembly when added to assembled tubulin. The concentration of amphethinile required to inhibit assembly by 50% (12 μ M) is very similar to that for colchicine (11 μ M). Amphethinile has been shown to be capable of competing for colchicine binding sites but not for those of the vinca alkaloids. Amphethinile can also be shown to stimulate the GTPase activity of tubulin in a manner similar to that observed for combretastatin A4 and 2-methoxy-5-(2',3',4'-trimethoxyphenyl) tropolone (MTPT) ^[1] . Amphethinile has been shown to cause a G2/M phase block in the cell cycle. In addition, this agent has been shown to be equally toxic toward parental and daunorubicin-resistant P388 cells. Whereas resistance in this cell line is associated with decreased drug accumulation in the case of daunorubicin, vincristine and vinblastine, this effect is much less pronounced for amphethinile ^[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pharmacokinetic studies in male mice are undertaken. Area under the curve values (AUC), show that levels of 313 μ g/L per hour are attained at doses equivalent to the LD ₁₀ . The alpha half life is 8 min after a bolus intravenous injection. The beta half life is 100 min and relatively independent of dose level ^[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay	The volume of methanol in the final incubation mixture is <1%, which does not modify the uptake of any of the drugs used in either drug sensitive or resistant lines. In addition, the same level of methanol is used in the control cultures. Drug incubations (10 μ M, 2h, 37°C) are performed in RPMI medium in the presence or absence of horse serum (10%). Cell suspensions (100 mL) are centrifuged (800 g, 10 min, 4°C), washed in PBS, lysed in distilled water by sonication, and the drug extracted into CHCl ₃ . The amphethinile concentration is determined spectrophotometrically ($\lambda=304$ nm) relative to a standard curve ^[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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**Animal
Administration**

Mouse: Initial toxicity studies on this agent are performed under contract in MFI-strain male mice following an acute i.v. and i.p. administration as well as a 4-weekly 5 day sub acute study. Preclinical toxicology is undertaken using the clinically formulated drug. The formulation consisted of 10 g amphetamine and 100 g Solutol HS15 diluted to 200 mL with 70% ethanolic citrate buffer at pH 6.0. The resulting drug concentration is 50mg mL^[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

- [1]. McGown AT, et al. Interaction of the novel agent amphetamine with tubulin. Br J Cancer. 1989 Jun;59(6):865-8.
[2]. McGown AT, et al. Pre-clinical studies of a novel anti-mitotic agent, amphetamine. Br J Cancer. 1988 Feb;57(2):157-9.
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Caution: Product has not been fully validated for medical applications. For research use only.

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