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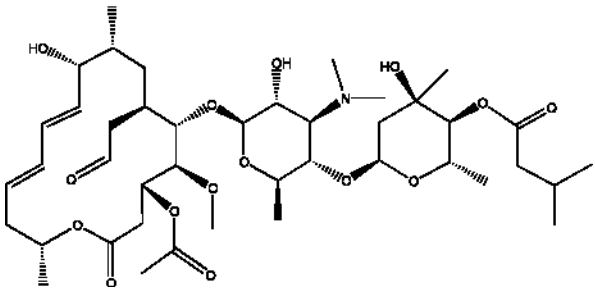
JOSAMYCIN

Therapeutic Function: Antibiotic

Chemical Name: Leucomycin V, 3-acetate-4β-(3-methylbutanoate)

Common Name: Josamycin; Leucomycin A3; Platenomycin A3; Turimycin A5; Yosamicina

Structural Formula:



Chemical Abstracts Registry No.: 16846-24-5

Trade Name	Manufacturer	Country	Year Introduced
Josalid	Biochemie	-	-
Josalid	Schering	-	-
Jomybel	Sarva	-	-
Josamina	Novag	-	-
Josamycin	Yamanouchi Pharmaceutical Co., Ltd.	-	-
Josamycin	Shanghai Lansheng Corporation	-	-
Vilprafen	Heinrich Mack	-	-
Proxacin	Yamanouchi	-	-

Raw Materials

Soybean meal	*Streptomyces narbonensis var. josatny ceticus*
Starch	Dipotassium hydrogen phosphate
Glucose	Magnesium sulfate
Sodium chloride	Hydrochloric acid
Sodium hydroxide	

Manufacturing Process

100 ml of a culture medium consisting of water containing 1.5% soybean meal, 1% starch, 1% glucose, 0.3% sodium chloride, 0.1% dipotassium hydrogen phosphate, and 0.05% magnesium sulfate was placed in a 500 ml flask and sterilized for 20 min at 120°C. After cooling, the culture medium was inoculated with strain A 205-P_2 *Streptomyces narbonensis var. josatny ceticus*, and the strain was subjected to shaking culture at 27°-29°C and at 130 strokes per min and 8 cm amplitude. After 3 days of culture, the culture fluids in such 100 flasks were combined together and filtered to give 8700 ml of culture filtrate. The pH of the filtrate was 6.4 and showed an inhibition zone of 25 mm. to Bacillus subtilis (PCI 219 strain). The filtrate was extracted with 8700 ml of ethyl acetate. The extract (7300 ml) thus obtained was concentrated to 730 ml under vacuum at temperatures lower than 50°C, 360 ml of water added, and then concentrated hydrochloric acid added to ad just the pH to 2.0, whereby josamycin was transferred to the aqueous layer. After adjusting the pH of the aqueous layer to 7.5 by the addition of 0.1 N sodium hydroxide, josamycin was extracted with 180 ml of ethyl acetate.

Josamycin was then transferred to 90 ml of an aqueous solution at pH 2.0 and extracted again with 45 ml of ethyl acetate as above process. Ethyl acetate solution thus obtained was evaporated under reduced pressure to give a solidified product, which was dissolved in 5 ml of benzene to remove impurities and the product, solidified from the benzene solution by evaporating under reduced pressure, was dissolved in a small amount of ethyl acetate and subjected to an alumina chromatography. That is, Brockman alumina (Merck) was treated with hydrochloric acid, sufficiently rinsed with water, and activated by heating for 5 h at 150°C.

50.0 g of thus treated alumina was filled in a glass tube of 1.6 cm in diameter by using ethyl acetate. The above prepared ethyl acetate solution was added to the alumina column and the product was eluted with 200 ml of ethyl acetate. The eluate thus obtained was concentrated under reduced pressure and the solid product thus obtained was dissolved in 5 ml of benzene and 50 ml of n-hexane added to give 0.18 g of amorphous josamycin having a purity of above 90%.

References

Umezawa H., Osono T.; US Patent No. 3,636,197; Jan. 18, 1972; Assigned: Yamanouchi Pharmaceutical Co., Ltd., Tokyo, Japan