W

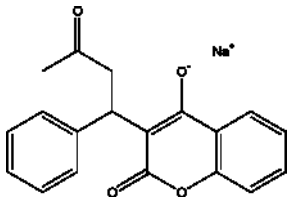
WARFARIN SODIUM

Therapeutic Function: Anticoagulant

Chemical Name: 3-(α-Acetonylbenzyl)-4-hydroxycoumarin sodium salt

Common Name: -

Structural Formula:



Chemical Abstracts Registry No.: 129-06-6; 81-81-2 (Base)

Trade Name	Manufacturer	Country	Year Introduced
Coumadin	Endo	US	1954
Prothromadin	Harvey	US	1956
Athrombin	Purdue Frederick	US	1959
Coumadine	Merrell	France	1959
Panwardin	Abbott	US	1960
Adoisine	Delalande	France	-
Aldocumar	Atdo Union	Spain	-
Dicusat	Ferrosan	Denmark	-
Marevan	Orion	Finland	-
Tintorane	A.C.F.	Netherlands	-
Waran	Nyegaard	Norway	-
Warcoumin	Harvey	Australia	-
Warfilone	Merck-Frosst	Canada	-

Raw Materials

4-Hydroxycoumarin
Benzalacetone
Sodium hydroxide

Manufacturing Process

About 0.1 mol each of 4-hydroxycoumarin and benzalacetone are dissolved, in any desired order, in about three times their combined weight of pyridine. The solution is refluxed for about 24 hours, and then allowed to cool; after which it is poured into about 15 volumes of water, and acidified to about pH 2 by the addition of hydrochloric acid. An oil separates, and on cooling and standing overnight solidifies. The solid product is recovered, as by filtration, and recrystallized from ethanol, according to US Patent 2,427,578.

The base melts at about 161°C. It is a white crystalline solid, soluble in hot ethyl alcohol and substantially insoluble in cold water; it dissolves in alkali solutions with formation of the salt. The yield is about 40%.

Then, as described in US Patent 2,777,859, warfarin may be reacted with NaOH to give a sodium salt solution. Crystalline warfarin sodium may be prepared as described in US Patent 2,765,321.

References

Merck Index 9852
Kleeman & Engel p. 950
PDR pp. 545, 852, 1606
OCDS Vol. 1 p. 331 (1977)
I.N. p. 1015
REM p. 827
Stahmann, M.A., Ikawa, M. and Link, K.P.; US Patent 2,427,578; September 16, 1947; assigned to Wisconsin Alumni Research Foundation
Schroeder, C.H. and Link, K.P.; US Patent 2,765,321; October 2, 1956; assigned to Wisconsin Alumni Research Foundation
Link, K.P.; US Patent 2,777,859; January 15, 1957; assigned to Wisconsin Alumni Research Foundation