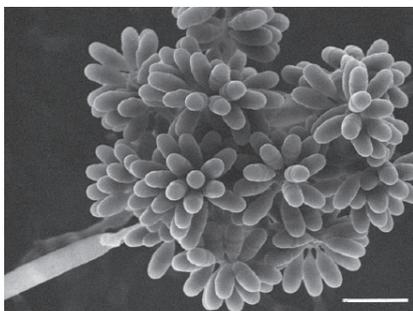


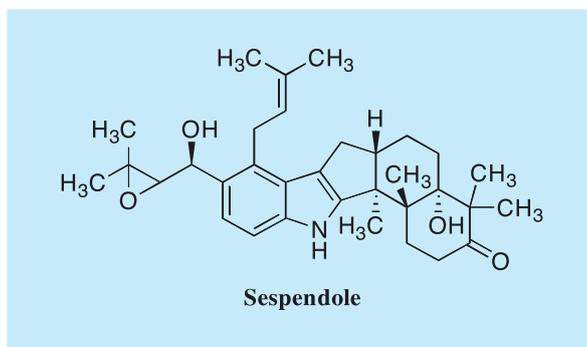
# Sespendole

## 1. Discovery, producing organism and structure<sup>1,3,4)</sup>

Sespendole was originally isolated from the culture broth of *Pseudobotrytis terrestris* (current name: *Cordana terrestris*) strain FKA-25 during chemical screening. Later it was found to show inhibitory activity against lipid droplet formation in macrophages.



*Pseudobotrytis terrestris* FKA-25  
(*Cordana terrestris* FKA-25)  
Bar: 10  $\mu\text{m}$

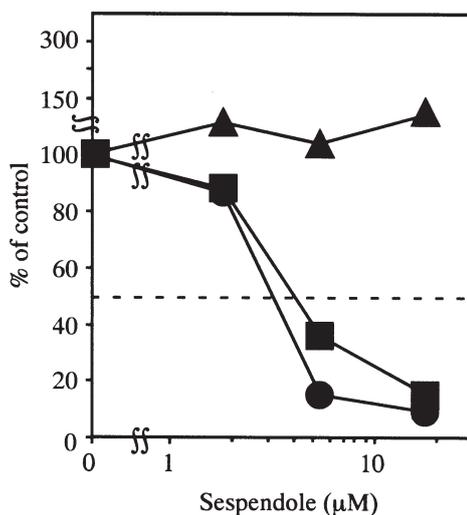


## 2. Physical data<sup>4)</sup>

White powder.  $\text{C}_{33}\text{H}_{45}\text{NO}_4$ ; mol wt 519.33. Sol. in MeOH, acetone, EtOH,  $\text{CHCl}_3$ . Insol. in  $\text{H}_2\text{O}$ , hexane.

## 3. Biological activity<sup>1,5)</sup>

- 1) Sespendole inhibited mouse macrophage synthesis of cholesteryl ester (CE) and triacylglycerol (TG) with  $\text{IC}_{50}$  values of 4.0 and 3.2  $\mu\text{M}$ .<sup>1)</sup>



Effects of sespendole on [ $^{14}\text{C}$ ]CE (■), [ $^{14}\text{C}$ ]TG (●) and [ $^{14}\text{C}$ ]PL (▲) synthesis in macrophages.

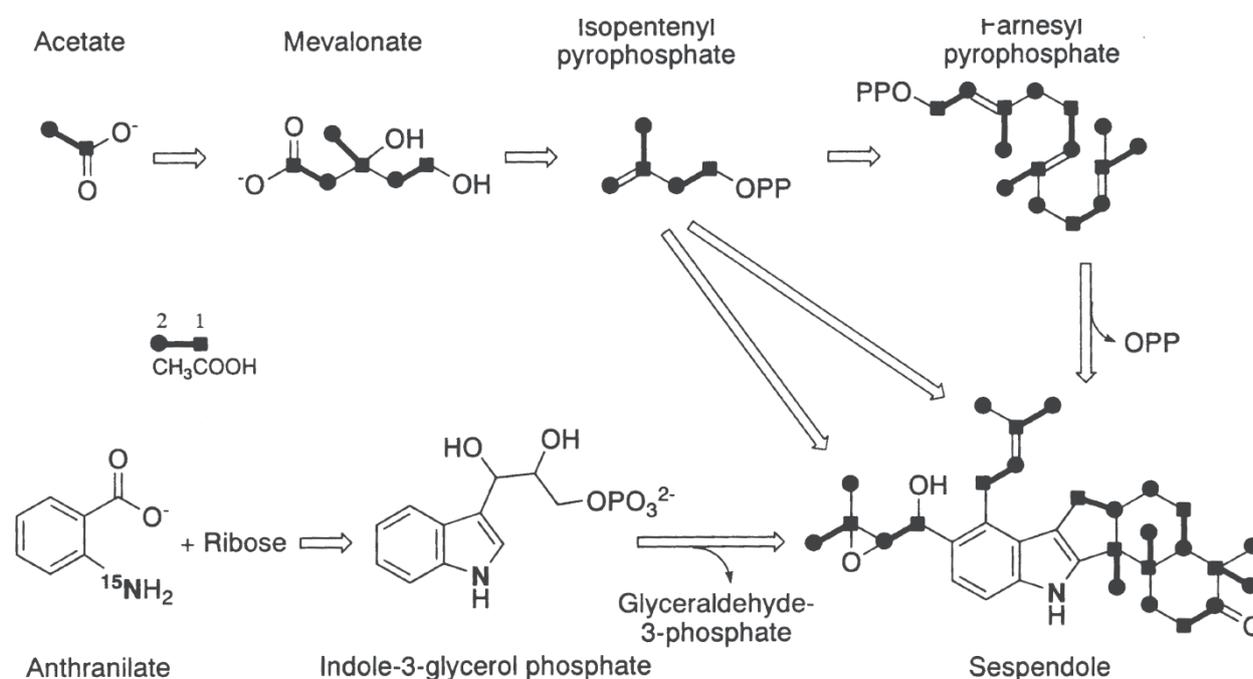
- 2) Suspendole inhibited both ACAT1 and ACAT2 activities with SI values of 1.7 to 1.8 in both cell based assay and enzyme assay.<sup>5)</sup>

	IC <sub>50</sub> for cholesteryl ester (CE) synthesis (μM)					
	Cell-based assay			Enzyme assay		
	ACAT1-CHO	ACAT2-CHO	SI	ACAT1	ACAT2	SI
Suspendole	12	6.5	1.8	20	12	1.7

- 3) Suspendole showed weak antimicrobial activity against *Bacillus subtilis* (inhibition zone, 7.0 mm, at 10 μg/6 mm disk) and *Mycobacterium smegmatis* (9.5 mm).<sup>1)</sup>

#### 4. Biosynthesis<sup>2)</sup>

The biosynthesis of suspendole was studied through feeding experiments with [<sup>13</sup>C]acetate, [<sup>15</sup>N] anthranilic acid and [<sup>13</sup>C]tryptophan. The data suggested the a farnesyl residue derived from the mevalonate pathway and an anthranilate-derived indole-3-glycerole residue are condensed, and then cyclization occurs, along with rearrangement to form the indololosesquiterpene core.



#### 5. References

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