# 生物策略表

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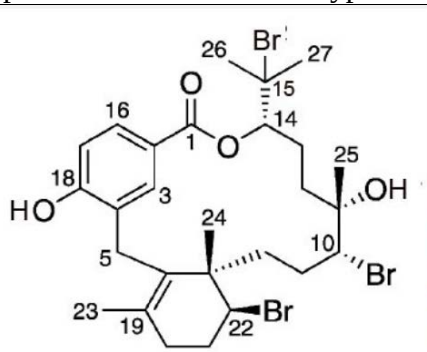
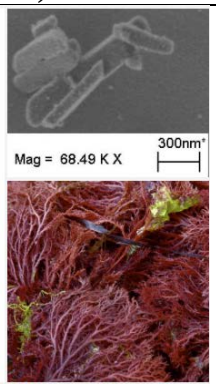
| **類別** | 生物策略 (Strategy) |
| **生物策略**<br>STRATEGY | 化合物干擾瘧疾寄生蟲<br>(Compounds disrupt malaria parasite) |
| **生物系統**<br>LIVING SYSTEM | 斐濟紅海藻 *Callophycus serratus*<br>(Fijian red seaweed) |
| **功能類別**<br>FUNCTIONS | #保護免受真菌危害 #保護免受微生物危害<br>#Protect from fungi #Protect from microbes |
| **作用機制標題** | 斐濟紅海藻中的 Bromophycolide 化合物，可透過干擾寄生蟲保護自身免受有毒副產物的能力，來提供抵抗瘧疾的保護<br>(Bromophycolide compounds in the Fijian red seaweed provide protection against malaria by interrupting the parasite's ability to protect itself from toxic byproducts.) |
| **生物系統/作用機制示意圖** |   |

**作用機制摘要說明** (SUMMARY OF FUNCTIONING MECHANISMS)

每年有超過一百萬人死於瘧疾 (malaria)，這是由屬於寄生蟲的瘧原蟲 (*Plasmodium falciparum*) 所引致。這種寄生蟲已經對多種抗瘧疾藥物產生出抗藥性，並開始對現今最重要的抗瘧疾藥物青蒿素 (artimisinin) 表現出抗藥性。這是非常嚴重的危機，因為世界上有一半的人口都曝露在這種疾病的風險之下。

多功能性 (multifunctionality) 是天然化合物的普遍特性。通常每種功能都被會生產該化合物的生物所使用，例如甲蟲的幾丁質 (chitin) 外層，同時提供了堅固的保護、防水、以及著色功用。

在斐濟紅海藻 (Fijian red seaweed) 的例子中，稱為 bromophycolide A 的有機化合物可作為抗真菌劑 (antifungal agent)。這種化合物同時亦能干擾引起瘧疾的寄生蟲瘧原蟲的代謝。雖然這對海藻本身不是問題，但對於有著紅血球的人類來說是個好消息，因為瘧原蟲會以我們攜帶氧氣的血紅蛋白 (hemoglobin) 為食。隨著瘧原蟲咀嚼血紅蛋白，游離的血基質 (heme) 會被釋放出來。瘧原蟲為了保護自己免受游離的血基質所毒害，會將其轉變成為無毒的瘧色素 (hemozoin)。 bromophycolide A 干擾了這個轉變，使瘧原蟲容易受害於這種殘留在餐桌上的劇毒碎屑。

化學家檢視了 bromophycolide A 的化學結構，來確定哪個修飾分子的官能基在抗瘧疾過程中起關鍵作用。似乎是第 15 位及第 18 位的碳原子（見結構圖）起了關鍵作用，前者的官能基不利於與游離血基質產生氫鍵，而第 18 位的碳則會促進此反應。這樣的結果將會對未來由 bromophycolide 啟發的抗瘧疾化合物的設計上提供見識。目前尚不清楚 bromophycolide 在抗真菌活性上是否使用類似的機制。

More than a million people die each year from malaria, which is caused by the parasite *Plasmodium falciparum*. The parasite has developed resistance to many antimalarial drugs and has begun to show resistance to artemisinin – today's most important antimalarial drug. The stakes are high because half of the world's population is at risk for the disease.

Multifunctionality is a common characteristic of natural chemical compounds. Often, each of the functions is utilized by the organism producing the compound, such as beetles' chitin-based covering that provides, among other functions, hard shielding, waterproofing, and coloring.

In the case of the Fijian red seaweed, an organic compound called bromophycolide A serves as an antifungal agent. This same compound also disrupts the metabolism of the malarial parasite, *Plasmodium falciparum*. While that's a non-issue for the seaweed itself, it's good news to red-blooded humans because the malarial parasite feasts on our oxygen-carrying hemoglobin. As the parasite masticates hemoglobin, free heme molecules are released. To protect themselves from the toxicity of free heme, the parasite transforms it into nontoxic hemozoin. It's this transformation that bromophycolide A disrupts, leaving the parasite vulnerable to the toxic crumbs left at its dining table.

Chemists have examined the chemical architecture of bromophycolide A to determine which functional groups decorating the molecule play key roles in the antimalarial process. It appears that carbon atoms at positions 15 and 18 (see structure diagram) play key roles, the former designed with functional groups that do not facilitate hydrogen bonding with free heme and carbon 18 designed to promote it. Such results will provide insight for potential future designs of bromophycolide-inspired antimalarial compounds. It is not clear at this time if the antifungal activity of bromophycolide uses a similar mechanism.

**文獻引用** (REFERENCES)

人類瘧疾的寄生蟲對發展中國家來說仍然是個重擔。它每年導致多達一百萬人死亡，這個數字可能還會上升，因為對於目前所有有效抗瘧疾藥物的多重藥物抗性 (multi-drug resistance) 正逐漸增加。(Cervantes et al. 2012: 1)

「熱帶海藻物種用作抵抗真菌侵襲的一組化合物，提供了對人類具有抗瘧疾的特性。這種化合物是被海藻用作對抗敵人的獨特的化學訊號系統的一部分，並可能提供了大量潛

在的新型製藥化合物。」 (Toon 2011: 1)

「我們觀察到當培養物加入經過純化的 bromophycolide A 萃取物進行一起培養時，有明顯的細胞週期停滯表型，以及缺乏癆色素的形成，因此使用純 bromophycolide A 也有相同效果。這些觀察指出了 bromophycolide A 的潛在作用方式可能阻止癆色素的形成。更進一步的研究使用了螢光香豆素 (coumarin) 標誌 bromophycolide A 作次細胞定位 (subcellular localization) 以及分子標耙識別 (molecular target identification)，研究驗證了血基質的結晶作用 (crystallization) 會被天然產物的 bromophycolide A 所干擾。」 (Cervantes et al. 2012: 8)

"The human malaria parasite remains a burden in developing nations. It is responsible for up to one million deaths a year, a number that could rise due to increasing multi-drug resistance to all antimalarial drugs currently available." (Cervantes et al. 2012: 1)

"A group of chemical compounds used by a species of tropical seaweed to ward off fungus attacks may have promising antimalarial properties for humans. The compounds are part of a unique chemical signaling system that seaweeds use to battle enemies – and that may provide a wealth of potential new pharmaceutical compounds." (Toon 2011: 1)

"We observed a distinct phenotype of cell cycle arrest and lack of hemozoin formation when cultures were incubated with extracts from which bromophycolide A was purified and thus pure bromophycolide A as well. These observations indicated that bromophycolide A's potential mode of action may prevent hemozoin formation. Further investigation using a fluorescent coumarin tagged bromophycolide A for sub-cellular localization and molecular target identification studies validated that heme crystallization was disrupted by the natural product bromophycolide A." (Cervantes et al. 2012: 8)

**參考文獻清單與連結** (REFERENCE LIST)

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(https://doi.org/10.1002/cmdc.201100252)

**延伸閱讀**

**生物系統延伸資訊連結** (LEARN MORE ABOUT THE LIVING SYSTEM/S)

https://en.wikipedia.org/wiki/callophycus_serratus
https://www.onezoom.org/life/@callophycus_serratus
https://eol.org/pages/905249

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**AskNature 原文連結**

https://asknature.org/strategy/compounds-disrupt-malaria-parasite/