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论文

# 疟疾防治药物的研究——Ⅺ.2,4-二氨基-6-(N-取代-对氯苄氨基)喹唑啉衍生物的合成及其抗疟作用

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摘要:

合成2,4-二氨基-6-(N-取代-对氯苄氨基)喹唑啉衍生物33个,经伯氏鼠疟原虫(*Plasmodium berghei*)抑制性治疗筛选,剂量20mg/kg×3d,有10个化合物(1,2,5～8,14,20,21,26)抑制率在90%以上。经约氏鼠疟原虫(*P.yoelii*)斯氏按蚊系统的病因性预防筛选,剂量5mg/kg×3d,有26个化合物(1～12,14,20～22,24～33)使小白鼠全部得到保护;剂量下降到0.625mg/kg×3d,有14个化合物(5～12,14,20,21,26,31,33)使小白鼠全部得到保护(表1)。4个化合物(1,8,20,25,表2,3)进行了猴疟(*P.cynomolgi*)试验,效果不及伯喹和乙胺嘧啶。

关键词:  抗疟作用  2,4-二氨基-6-取代氨基喹唑啉  抑制性治疗  病因性预防

## STUDIES ON ANTIMALARIALS XI. SYNTHESIS AND ANTIMALARIAL ACTIVITIES OF SOME 2, 4-DIAMINO-6-(N-SUBSTITU-TED-P-CHLOROBENZYLAMINO) QUINAZOLINE DERIVATIVES

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Abstract:

Thirty three 2, 4-diamino-6-(N-substituted-p-chlorobenzylamino)-quinazolines were synthesized. These compounds were prepared by treatment of 2, 4-diamino-6-p-chlorobenzylamino quinazoline(Ⅰ) with acyl chloride, sulfonyl chloride, isosulfocyanate or acrylonitrile, the corresponding compounds(20～30) were obtained respectively. Some substituted amino methyl compounds(31～33) were prepared by Mannich reaction of(Ⅰ). Moreover, the nitroso derivative(5) of(Ⅰ) through reduction afforded amino-compound(14) which was condensed with the appropriate benzaldehyde to give the requisite Schiff bases(15～19).Suppressive therapeutic tests in mice infected with *Plasmodium berghei* showed that ten(1, 2, 5～8, 14, 20, 21, 26) out of these compounds produced 90% suppression of the parasites when administered orally at dose of 20 mg/kg/d × 3. Twenty six compounds(1～12, 14, 20～22, 24～33) given orally at dose of 5 mg/kg/d × 3 were shown to possess causal prophylactic activity against *P. yoelii* in mice. When the regimen was reduced to 0.625 mg/kg/d × 3 thirteen compounds(5～12, 20, 21, 26, 31, 33) were shown to prevent the test mice from being infected. In tests against *P. cynomolgi* in rhesus monkeys, four compounds(1, 8, 20, 25) were found to be less effective than primaquine and pyrimethamine in the same dosage level.

Keywords: 2,4-Diamino-6-substituted quinazolines  Suppressive therapeutic effects  Causal prophylactic activity  Antimalarial

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