Studies on synthesis and antiviral activities of a novel acyclic nucleoside phosphonates analogues on HBV

QIU Xiao, LIU Jia, FENG Ji, NIU Chun, LIKe (Department of Medical Chemistry, School of Pharmacy, Second Military Medical University, Shanghai 200433, China)

[Abstract] Objective To study the design and synthesis of the novel acyclic nucleoside phosphonates analogues and study their activities of inhibiting HBV. Methods Based on the chemical structure of PMEA, and according to the theory of bioisostere, a 8aza 6 thiophenyl group was introduced and a series of title compounds were synthesized. All of them were confirmed by IR, 1H NMR and MS. Preliminary pharmacological test of compounds 1a 1e was made on HBV. Results Ten compounds were synthesized. The test results show the inhibitory rate of 1a 1e compounds on HBsAg and HBeAg is higher than PMEA. The inhibitory rate of compound 1e on HBV DNA is correspond with PMEA. Conclusion The PMEA derivatives with a 8aza 6 thiophenyl group have high activity on inhibiting HBsAg HBeAg and HBV DNA.

[Keywords] acyclic nucleoside phosphonates; chemical synthesis; PMEA; Antihepatitis B virus activity

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\[ 6 \xrightarrow{N_{H}} 5 \xrightarrow{O_{H}} 4 \xrightarrow{V} 1a-1e \]

\[ 3a-3e \xrightarrow{\text{III}} \]

\[ 1a-1e \]

\[ a = R = \text{CH}_3; b = R = \text{Br}; c = R = F; d = R = \text{Cl}; e = R = \text{CH}(\text{CH}_3)_2 \]

\[ \text{NaNO}_2/\text{CH}_3\text{CN} ; \text{NH} \text{NO}_3/\text{CH}_3\text{COOH} ; \text{NH}_2/\text{DMF} / \text{P TpCH}_2\text{POO} (\text{OC}_2\text{H}_5)_2 ; \text{HCl} \text{Cl} \]

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