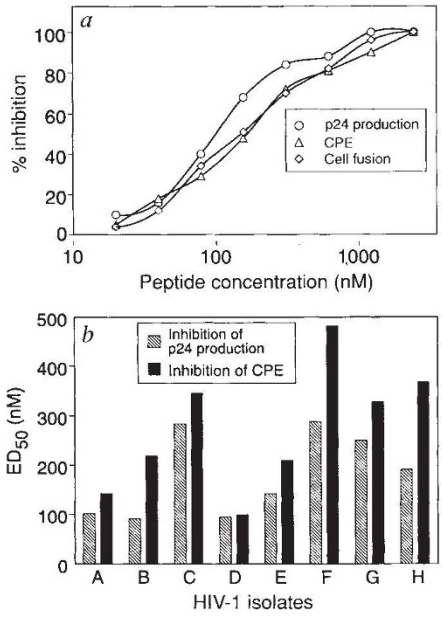
HIV-1 inhibition by a peptide

SIR — Studies on interactions between the domains of peptides involved in assembly of some enveloped RNA viruses suggest that peptides from virus envelope glycoproteins have antiviral activity[1]. A peptide from HIV-1 gp41 (DP-107: NNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQ) has antiviral activity[2], for example. We have found that a peptide from another gp41 region (amino-acid residues 637–666: EWDREINNYTSLIHSLIEESQNQQEKNEQE*GGC*) also strongly inhibits HIV-1-IIIB replication. The 50% effective doses (ED_{50}) for inhibition of gag p24 nucleocapsid protein production, the cytopathogenic effect (CPE) and cell fusion were 101, 142 and 156 nM, respectively (*a* in the figure). HIV-1 infection was completely inhibited at concentrations of peptide greater than 2 μM.



Inhibition by peptide (637–666) of infection by *a*, HIV-1-IIIB and *b*, by different isolates: IIIB (A); MN (B); RF (C); SF2 (D); V32 (E); and HIV-1 sensitive (F), partially resistant (G), and resistant to AZT (H). Infection of MT-2 cells by HIV-1-IIIB or by other HIV-1 isolates (multiplicity of infection 0.0045) in the presence or absence of the peptide (637–666) was detected by ELISA for p24 production and a colorimetric assay for CPE as previously described[5]. Cell fusion was measured as follows: HIV-1-IIIB infected H9 cells were labelled by 2′,7′-bis-(2-carboxyethyl)-5-(and-6)-carboxyfluorescein acetoxymethyl ester (BCECF-AM; Molecular Probes, Inc.) according to the manufacturer's instructions, and mixed with uninfected MT-2 cells. After incubation, the fused and unfused BCECF-labelled H9/HIV-1-IIIB cells were counted under an inverted fluorescence microscope and the per cent inhibition of cell fusion was calculated. HIV-1 V32 was provided by P. L. Nara; all other HIV-1 isolates were obtained from the NIH AIDS Research & Reference Reagent Program.

Peptide (637–666) inhibits infection by other HIV-1 strains: MN; RF; SF2; V32 (a IIIB variant resistant to neutralization by antibodies directed against the IIIB V3 loop of gp120, ref. 3); and HIV-1 derived from clinical isolates differing in sensitivity to AZT[4] (*b* in the figure). These results suggest that the peptide has antiviral activity against both homologous and heterologous HIV-1.

We synthesized the peptide (637–666) with a *GGC* linker at its carboxy terminus for convenience of peptide coupling to carriers or labelling. Mass spectrometric data (provided by B. T. Chait and U. Mirza, Rockefeller University) demonstrated that peptide (637–666) is dimerized. The monomeric form of (637–666), prepared by reduction with 1% 2-mercaptoethanol and alkylation with 3% iodoacetamide, has ED_{50} values for inhibition of p24 production, CPE and cell fusion, respectively, 3 to 4 times higher than those corresponding to the dimeric (637–666) peptide.

The peptide (637–666) has no detectable cytotoxicity for various cell lines tested or for peripheral blood lymphocytes and monocytes at a concentration of 816 μM, about 8,000 times higher than the ED_{50} values. Fresh sera from HIV-1-negative individuals did not interfere with the anti-HIV-1 activity of the peptide. The presence of antibodies recognizing this peptide in sera of HIV-1-infected individuals is not expected to interfere with antiviral activity, as the effective peptide concentration greatly exceeds the concentration of such antibodies. Furthermore, unconjugated peptide is not expected to elicit antibodies, particularly when administered without an adjuvant.

The mechanism by which the peptide (637–666) inhibits HIV-1 infection is under investigation. The peptide did not inhibit binding of HIV-1 to target cells but selectively bound to the virus fusion domain, suggesting that it inhibits HIV-1 infection by preventing the interaction between the fusogenic domain of gp41 and relevant cell membrane constituents, thereby blocking fusion of HIV-1 with cells or of infected cells with uninfected cells.

In summary, the peptide (637–666) has antiviral activity against both homologous and heterologous HIV-1 isolates and has no detectable cytotoxicity. It thus offers another approach to attempts to devise treatments for AIDS.

Shibo Jiang
Kang Lin
Nathan Strick
A. Robert Neurath
New York Blood Center,
New York,
New York 10021, USA

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Nested fullerene-like structures

SIR — Hollow carbon structures consisting of nested graphitic shells have been reported for various geometries[1–3], and the filling of these structures with metal compounds has also been described[4–6]. Our discovery[7] that similar hollow structures can be observed for the layered semiconductor tungsten disulphide leads one to expect that these structures might be formed from other layered materials. We have now found that molybdenum disulphide will also form such concentric structures, and that they too can be filled with metal compounds.

We deposited molybdenum films of 20 nm thickness onto quartz substrates, oxidized them at 500–600 °C in open air and fired them at 850–1,050 °C in a stream of H_2S and N_2/H_2 mixture. We peeled the MoS_2 films obtained off the substrate and examined them in the transmission electron microscope.

The figure (*a*) shows the lattice image of a few nested shells of MoS_2. The nested shells seem to be hollow in most cases. We also saw, albeit rarely, 'stuffed' structures, composed of molybdenum-dense core (confirmed by local energy dispersive X-ray analysis) wrapped with a few MoS_2 layers (inset in figure). X-ray photoelectron spectroscopy analysis of the films reveals a Mo:S atomic ratio of 1:2. This result indicates that the oxide serves as a precursor for the generation of a nested shell, rather than being a part of it.

We observed various apex angles, predominantly 120° and larger, but often of 60, 75 and 90°. Tilting about different axes shows that these angles are not necessarily symmetrical.

Some of the apex angles can be deduced from the MoS_2 layer structure. The figure (*b*, *c*, *d*) demonstrates how an apex can be created by folding and joining either three or four hexagons around a triangle or rhombus, respectively. Further growth of the cone may be explained by a model described by Kroto[8] for carbon fullerenes. Only one point defect — a molybdenum vacancy — is required for initiating this process. The generation of the 'stuffed' shells can be ascribed to a wrapping mechanism of spiral growth[9].

Structural transformations in the films