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Complexes assembled from TMV-derived spherical particles and entire virions of heterogeneous nature

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Previously, we described some structural features of spherical particles (SPs) generated by thermal remodelling of the tobacco mosaic virus. The SPs represent a universal platform that could bind various proteins. Here, we report that entire isometric virions of heterogeneous nature bind non-specifically to the SPs. Formaldehyde (FA) was used for covalent binding of a virus to the SPs surface for stabilizing the SP—virus complexes. Transmission and high resolution scanning electron microscopy showed that the SPs surface was covered with virus particles. The architecture of SP–virion complexes was examined by immunologic methods. Mean diameters of SPs and SP–human enterovirus C and SP–cauliflower mosaic virus (CaMV) compositions were determined by nanoparticle tracking analysis (NTA) in liquid. Significantly, neither free SPs nor individual virions were detected by NTA in either FA-crosslinked or FA-untreated compositions. Entirely, all virions were bound to the SPs surface and the SP sites within the SP–CaMV complexes were inaccessible for anti-SP antibodies. Likewise, the SPs immunogenicity within the FA-treated SPs–CaMV compositions was negligible. Apparently, the SP antigenic sites were hidden and masked by virions within the compositions. Previously, we reported that the SPs exhibited adjuvant activity when foreign proteins/epitopes were mixed with or crosslinked to SPs. We found that immunogenicity of entire CaMV crosslinked to SP was rather low which could be due to the above-mentioned masking of the SPs booster. Contrastingly, immunogenicity of the FA-untreated compositions increased significantly, presumably, due to partial release of virions and unmasking of some SPs-buster sites after animals immunization.

Keywords: tobacco mosaic virus; spherical particles; platforms; isometric viruses; immunogenic compositions

Introduction

Native tobacco mosaic virus (TMV) particles are rigid rod-like tubules (18 × 300 nm) composed of about 2130 of helically arranged coat protein (CP) subunits and RNAs which follow the CP helix at a radius of 4 nm (for review, see Caspar, 1963). Previously, we have described in detail the spherical particles (SPs) generated by thermal remodelling of native TMV at 94 °C. The SPs consist of thermally denatured TMV CP molecules, do not contain RNA, and are water insoluble and heterogeneous in size but uniform in shape. The size of SPs depended on virus concentration and, therefore, could be controlled. The SPs are water insoluble and highly stable (Atabekov, Nikitin, Arkhipenko, Chirkov, & Karpova, 2011; Nikitin et al., 2011).

Using circular dichroism, fluorescence spectroscopy and Raman spectroscopy, we found that the structure of SPs protein differs strongly from that of the native TMV and is characterized by CP subunits transition from mainly α-helical structure (of about 50%) to a structure with low content of α-helices and a significant fraction of β-sheets. In addition, our results suggested that TMV-to-SPs transition was accompanied by changes in the nature of amino acid residues exposed on the particles surface (Dobrov et al., 2013).

Several plant viruses have been developed as vectors for the production of vaccines by constructing chimeric CP subunits and presentation of foreign epitopes on the surface of a chimeric virus or RNA-free virus-like particles (VLPs). The chimeric multisubunit particles carrying foreign epitopes on their surface may be obtained either by *in vitro* assembly of VLPs from recombinant CP subunits fused to a heterologous foreign epitope or by *in vivo* expression of a full-length recombinant infectious viral genome containing the CP gene fused to a foreign

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