(acrylate carrier), Sepharose CL4B or Rapid Run Agarose Beads (cross-linked agarose carrier), Cellufine (cross-linked cellulose carrier) and the like.

[0045]

In addition, the water-insoluble carrier used in the first embodiment and the second embodiment of the present invention has desirably a large surface area and is preferably a porous matrix having a large number of fine pores with a suitable size, from the viewpoint of productivity to be treated per unit time. The carrier may be any form such as bead, monolith, fiber, or membrane (including hollow fiber), and the carrier can be selected from any form of these. The water-insoluble carrier is preferably a porous bead because the separation matrix can effectively function by ~~concertedly working the affinity ligand and the cation exchange group arranged on the water-insoluble carrier, causing proximity of physical distance between the affinity ligand and the cation exchange group, and~~ obtaining a given contact time. ~~When the cation exchange group is immobilized on the carrier to which the affinity ligand is fixed, a carrier made of polysaccharides or modified with monosaccharides or polysaccharides is preferable from the viewpoint of easy of introduction of the affinity ligand.~~ Concretely, the carrier is not particularly limited, and is preferably an agarose carrier and a cellulose carrier.

[0046]

In the first embodiment of the present invention, as a method for immobilizing the affinity ligand to the water-insoluble carrier or the separation matrix, a general method can be used. For example, an amino group of the affinity ligand may bind to a carrier via a formyl

group introduced on the carrier, and an amino group of the affinity ligand may bind to a carrier via an activated carboxyl group on the carrier. In addition, these water-insoluble carriers are activated so that the ligand can covalently bind to the carrier before introduction of the affinity ligand. A commercially available activated carrier may be used, and activation may be carried out by an operator himself/herself.

[0047]

In the first embodiment of the present invention, a functional group introduced to the water-insoluble carrier by activation is not specifically limited, so long as the functional group can form a covalent bond with the affinity ligand. Examples of the functional group may include a reactive functional group ("activating group") such as an epoxy group (epichlorohydrin), a hydroxy group activated by cyanogen bromide, N,N-disuccinimidyl carbonate (DSC) and the like, an aldehyde group or an activated carboxylic acid group (for example, N-hydroxysuccinimide (NHS) ester, carbonyldiimidazole (CDI) activated ester), and the like (Hermanson G.T. et al, "Immobilized Affinity Ligand Techniques, Academic Press", 1992, US 5,874,165, US 3,932,557, US 4,772,653, US 4,210,723, US 5,250,613, EP 13 52957, WO 2004/074471). These functional groups include a functional group in which the affinity ligand directly, covalently binds to the carrier, and a functional group in which a linear, branched, or cyclic linker or spacer is used. ~~Moreover, when the carrier to which the affinity ligand is introduced is activated, it is preferably activated by the technique in which the activated group directly does not react to the ligand.~~

[0048]