

mate pH of 6.0 to 7.5, yielding the anti-adhesion composition, Compound 22. The by-product, 2,4-dinitrophenoxide, is nominally non-toxic, and may be removed, for example, by washing, if desired. This anti-adhesion composition, Compound 22, is then reacted with receptive tissue. The nitrovinyl group of the DNPNVB moiety (e.g., possessing an activated double bond), acting as a tissue-selective group, reacts at the carbon alpha to the nitro group with free sulfhydryl groups (—SH) found in compounds of receptive tissue (for example, fibrin or other sulfhydryl-containing tissue macromolecule) to form a covalent sulfide linkage (—S—) to the tissue compounds.

Example 7

Use of an Anti-Adhesion Binding Agent With "Azido" and "Haloacetyl" Groups: ASIB

A flow chart which illustrates the preparation and use of an anti-adhesion binding composition comprising the titled anti-adhesion binding agent is shown in FIG. 9. ASIB (1-(p-azidosalicylamido)-4-(iodoacetamido)butane, Compound 23) is first reacted with collagen. The azide group of the ASIB, acting as a collagen-reactive functional group, is heat or light activated to yield a highly reactive —N group (and the by-product, gaseous nitrogen), which reacts with chemical bonds found in collagen (including, for example, C—H and C=C) to form secondary amine linkages (—NH—) (yielding the anti-adhesion composition, Compound 24) or with carbon-carbon double bonds (C=C) found in collagen to form a cyclic aziridine-like linkage (e.g., —N[—C—C—]). This anti-adhesion composition, Compound 24, is then reacted with receptive tissue. The iodoacetyl group of the ASIB moiety (e.g., possessing a haloacetyl group), acting as a tissue-selective group, reacts with free sulfhydryl groups (—SH) found in compounds of receptive tissue (for example, fibrin or other sulfhydryl-containing tissue macromolecule) at pH 6.5 to 7.5 to form a covalent sulfide linkage (—S—) to the tissue compounds. Again, the by-product, iodide ion, is nominally non-toxic. Other haloacetyl groups may be used as tissue-selective groups, such as bromoacetyl and chloroacetyl groups.

Yet another anti-adhesion binding agent, APDP (N-[4-(p-azidosalicylamido) butyl]-3'-(2'-pyridyldithio)propionamide, Compound 25), which possesses "disulfide" and "azide" groups, may be used in an analogous manner to obtain results similar to those for other disulfide and azide groups described above.

What is claimed is:

1. An anti-adhesion composition for treatment of receptive tissue comprising:

- (i) a substrate material; and
- (ii) an anti-adhesion binding agent, wherein said anti-adhesion agent further comprises a substrate-reactive functional group and a tissue-selective functional group.

2. The anti-adhesion composition of claim 1, wherein said substrate material comprises collagen.

3. The anti-adhesion composition of claim 1, wherein said tissue-selective group is a sulfhydryl-selective functional group.

4. The anti-adhesion composition of claim 2, wherein said binding agent comprises a derivative of polyethylene glycol.

5. The anti-adhesion composition of claim 3, wherein said sulfhydryl-selective functional group is selected from the group consisting of:

- (i) a disulfide group;
- (ii) a haloacetyl group;
- (iii) a halomethyl ester group;
- (iv) a β -Nitrovinyl group;
- (v) an N-hydroxy succinimidyl ester group; and
- (vi) a maleimidyl group.

6. The anti-adhesion composition of claim 5, wherein said sulfhydryl-selective functional group is selected from the group consisting of:

- (i) a disulfide group;
- (ii) a haloacetyl group;
- (iii) a halomethyl ester group; and
- (iv) a β -Nitrovinyl group.

7. The anti-adhesion composition of claim 6, wherein said sulfhydryl-selective functional group is a disulfide group.

8. The anti-adhesion composition of claim 7, wherein said disulfide group is a 2-pyridinyl-disulfide group or a 3-carboxylic acid-4-nitro-phenyl-disulfide group.

9. The anti-adhesion composition of claim 5, wherein said substrate-reactive functional group is selected from the group consisting of:

- (i) an active ester group;
- (ii) a haloacetyl group;
- (iii) an azide group;
- (iv) a haloformate group;
- (v) a sulfonyl halide group;
- (vi) an isocyanate group;
- (vii) an isothiocyanate group;
- (viii) an acid anhydride group;
- (ix) an acid halide group; and
- (x) an imidate ester group.

10. The anti-adhesion composition of claim 5, wherein said substrate-reactive functional group is selected from the group consisting of:

- (i) an active ester group;
- (ii) a haloacetyl group; and
- (iii) an azide group.

11. The anti-adhesion composition of claim 1, wherein said tissue-selective functional group is an amine-selective functional group.

12. The anti-adhesion composition of claim 1, wherein said tissue-selective functional group is an active ester group.

13. The anti-adhesion composition of claim 2, wherein said tissue-reactive functional group is an active ether group.

14. The anti-adhesion composition of claim 11, wherein said amine-selective functional group is selected from the group consisting of an active ester group, an active ether group, and combinations thereof.

15. The anti-adhesion composition of claim 4, wherein said substrate-reactive functional group is an active ester group.

16. The anti-adhesion composition of claim 4, wherein said substrate-reactive functional group is an active ether group.

17. The anti-adhesion composition of claim 5 wherein said substrate-reactive functional group is an N-succinimidyl active ester group or a 2,4-dinitrophenyl active ester.

18. An anti-adhesion device for treatment of receptive tissue, said device comprising at least one layer of substrate material covalently bonded to an anti-adhesion binding agent, wherein said anti-adhesion agent further comprises a tissue-selective functional group.