WHAT WE CLAIM

~~1. An antibody molecule capable of neutralizing the activity of an anticoagulant.~~

~~2. The antibody molecule of claim 1 wherein said antibody molecule has binding specificity for the anticoagulant.~~

~~3. The antibody molecule of claim 1 or 2 wherein the anticoagulant is a direct thrombin inhibitor, a Factor Xa inhibitor, or a vitamin K antagonist.~~

~~4.~~1. An antibody molecule capable of neutralizing the activity of ~~The antibody molecule of any one of the preceding claims, wherein the anticoagulant is~~ dabigatran, ~~argatroban, melagatran, ximelagatran, hirudin, bivalirudin, lepirudin, desirudin, apixaban, otamixaban, rivaroxaban, defibrotide, ramatroban, antithrombin III, or drotrecogin alpha~~which comprises a heavy chain variable domain with a CDR1 of SEQ ID NO: 1, a CDR2 of SEQ ID NO: 7, and a CDR3 of SEQ ID NO: 10, and a light chain variable domain with a CDR1 of SEQ ID NO: 13, a CDR2 of SEQ ID NO: 14, and a CDR3 of SEQ ID NO: 15.

~~5. The antibody molecule of any one of the preceding claims, wherein the anticoagulant is a disubstituted bicyclic heterocycle of of general formula~~

~~R_a - A - Het - B - Ar - E , (I)~~

~~wherein~~

~~A denotes a carbonyl or sulphonyl group linked to the benzo, pyrido or thieno moiety of the group Het,~~

~~B denotes an ethylene group in which the methylene group linked to the group Ar may be replaced by an oxygen or sulphur atom or by an $-NR_4-$ group, wherein~~

~~R_4 denotes a hydrogen atom or a C_{1-4}-alkyl group,~~

~~E denotes an $R_bNH-C(=NH)-$ group wherein~~

R_b denotes a hydrogen atom, a hydroxy, C_{1-9}-alkoxycarbonyl, cyclohexyloxycarbonyl, phenyl-C_{1-3}-alkoxycarbonyl, benzoyl, p-C_{1-3}-alkyl-benzoyl or pyridinoyl group, whilst the ethoxy moiety in the 2-position of the abovementioned C_{1-9}-alkoxycarbonyl group may additionally be substituted by a C_{1-3}-alkylsulphonyl or 2-(C_{1-3}-alkoxy)-ethyl group,

Ar denotes a 1,4-phenylene group optionally substituted by a chlorine atom or by a methyl, ethyl or methoxy group or it denotes a 2,5-thienylene group,

Het denotes a 1-(C_{1-3}-alkyl)-2,5-benzimidazolylene, 1-cyclopropyl-2,5-benzimidazolylene, 2,5-benzothiazolylene, 1-(C_{1-3}-alkyl)-2,5-indolylene, 1-(C_{1-3}-alkyl)-2,5-imidazo[4,5-b]pyridinylene, 3-(C_{1-3}-alkyl)-2,7-imidazo[1,2-a]pyridinylene or 1-(C_{1-3}-alkyl)-2,5-thieno[2,3-d]imidazolylene group and

R_a denotes an R_2NR_3- group wherein

R_2 is a C_{1-4}-alkyl group which may be substituted by a carboxy, C_{1-6}-alkyloxycarbonyl, benzyloxycarbonyl, C_{1-3}-alkylsulphonylaminocarbonyl or 1H-tetrazol-5-yl group,

a C_{2-4}-alkyl group substituted by a hydroxy, benzyloxy, carboxy-C_{1-3}-alkylamino, C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino, N-(C_{1-3}-alkyl)-carboxy-C_{1-3}-alkylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino group, whilst in the abovementioned groups the carbon atom in the α-position to the adjacent nitrogen atom may not be substituted,

R_3 denotes a C_{3-7}-cycloalkyl group, a propargyl group, wherein the unsaturated part may not be linked directly to the nitrogen atom of the R_2NR_3 group, a phenyl group optionally substituted by a fluorine or chlorine atom, or

by a methyl or methoxy group, a pyrazolyl, pyridazolyl or pyridinyl group optionally substituted by a methyl group or

R_2 and R_3 together with the nitrogen atom between them denote a 5- to 7-membered cycloalkyleneimino group, optionally substituted by a carboxy or C_{1-4}-alkoxycarbonyl group, to which a phenyl ring may additionally be fused,

the tautomers, the stereoisomers and the salts thereof.

6. The antibody molecule of claim 5, wherein the anticoagulant is a compound selected from

(a) 2-[N-(4-amidinophenyl)-aminomethyl]-benzthiazole-5-carboxylic acid-N-phenyl-N-(2-carboxyethyl)-amide,

(b) 2-[N-(4-amidinophenyl)-N-methyl-aminomethyl]-benzthiazol-5-yl-carboxylic acid-N-phenyl-N-(2-hydroxycarbonylethyl)-amide,

(c) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-(2-hydroxycarbonylethyl)-amide,

(d) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-(3-hydroxycarbonylpropyl)-amide,

(e) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(hydroxycarbonylmethyl)-amide,

(f) 1-Methyl-2-[2-(2-amidinothiophen-5-yl)ethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(g) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(h) 1-Methyl-2-[2-(4-amidinophenyl)ethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(i) 1-Methyl-2-[2-(4-amidinophenyl)ethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-(2-hydroxycarbonylethyl)-amide,

(j) 1-Methyl-2-[2-(4-amidinophenyl)ethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-[2-(1H-tetrazol-5-yl)ethyl]-amide,

(k) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-[2-(1H-tetrazol-5-yl)ethyl]-amide,

(l) 1-Methyl-2-[N-(4-amidinophenyl)-N-methyl-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(m) 1-Methyl-2-[N-(4-amidinophenyl)-N-methyl-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(3-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(n) 1-Methyl-2-[N-(4-amidinophenyl)-N-methyl-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-(2-hydroxycarbonylethyl)-amide,

(o) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-[(N-hydroxycarbonylethyl-N-methyl)-2-aminoethyl]-amide,

(p) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(3-fluorophenyl)-N-(2-hydroxycarbonylethyl)-amide,

(q) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(4-fluorophenyl)-N-(2-hydroxycarbonylethyl)-amide,

(r) 1-Methyl-2-[N-(4-amidino-2-methoxy-phenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-(2-hydroxycarbonylethyl)-amide,

~~(s) 1-Methyl-2-[N-(4-amidino-2-methoxy-phenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,~~

~~(t) 1-Methyl-2-[N-(4-amidinophenyl)aminomethyl]-indol-5-yl-carboxylic acid-N-phenyl-N-(2-methoxycarbonylethyl)-amide and~~

~~(u) 1-Methyl-2-[N-(4-amidinophenyl)aminomethyl]-thieno[2.3-d]imidazol-5-yl-carboxylic acid-N-phenyl-N-(2-hydroxycarbonylethyl)-amide,~~

~~(v) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-phenyl-N-(2-hydroxycarbonylethyl)-amide,~~

~~(w) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,~~

~~(x) 1-Methyl-2-[N-(4-amidino-2-methoxy-phenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,~~

~~(y) 1-Methyl-2-[N-[4-(N-n-hexyloxycarbonylamidino)phenyl]-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-ethoxycarbonylethyl)-amide,~~

~~the tautomers, stereoisomers and the salts thereof.~~

~~7. The antibody molecule of claim 2 wherein the anticoagulant is dabigatran.~~

~~8.~~2. The antibody molecule of claim ~~7~~ 1 which is capable of neutralizing the activity of dabigatran and 1-O-acylglucuronide of dabigatran.

~~9. The antibody molecule of any one of claims 5 to 8 which comprises a heavy chain variable domain with a CDR1 selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2, a CDR2 selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8, and a CDR3 selected from the group consisting of SEQ ID NO: 9 and SEQ ID NO:~~

~~10, and a light chain variable domain with a CDR1 selected from the group consisting of SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 13, a CDR2 of SEQ ID NO: 14, and a CDR3 of SEQ ID NO: 15.~~

~~10. The antibody molecule of claim 9 which comprises a heavy chain variable domain with a CDR1 of SEQ ID NO: 1, a CDR2 selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8, a CDR3 of SEQ ID NO: 10, and a light chain variable domain with a CDR1 of SEQ ID NO: 13, a CDR2 of SEQ ID NO: 14, and a CDR3 of SEQ ID NO: 15.~~

~~11.~~3. The antibody molecule of claims ~~9~~ 1 or ~~10~~ 2 which comprises a heavy chain variable domain ~~selected from the group consisting~~ of SEQ ID NO~~s~~: ~~16, 18, 20, 22,~~ 24~~, and 26,~~ and a light chain variable domain ~~selected from the group consisting~~ of SEQ ID Nos: ~~17, 19, 21, 23, 25, and~~ 27.

~~12. The antibody molecule of claim 11 which comprises a heavy chain variable domain of SEQ ID NO: 16, and a light chain variable domain of SEQ ID No: 17, or a heavy chain variable domain of SEQ ID NO: 18, and a light chain variable domain of SEQ ID No: 19, or a heavy chain variable domain of SEQ ID NO: 20, and a light chain variable domain of SEQ ID No: 21, or a heavy chain variable domain of SEQ ID NO: 22, and a light chain variable domain of SEQ ID No: 23, or a heavy chain variable domain of SEQ ID NO: 24, and a light chain variable domain of SEQ ID No: 25, or a heavy chain variable domain of SEQ ID NO: 24, and a light chain variable domain of SEQ ID No: 27, or a heavy chain variable domain of SEQ ID NO: 26, and a light chain variable domain of SEQ ID No: 27.~~

~~13.~~4. The antibody molecule of any one of the preceding claims which is a ~~polyclonal antibody, a~~ monoclonal antibody, a human antibody, a humanized antibody, a chimeric antibody, a fragment of an antibody, in particular a Fab, Fab', or $F(ab')_2$ fragment, or a single chain antibody, in particular a single chain variable fragment (scFv)~~, a Small Modular Immunopharmaceutical (SMIP), a domain antibody, a nanobody, a diabody, or a Designed Ankyrin Repeat Protein (DARPin)~~.

~~14.~~5. The antibody molecule of claim ~~13~~ 4 which is a scFv, wherein the heavy chain variable domain and the light chain variable domain are linked to each other through a linker peptide selected from the group consisting of SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, and SEQ ID NO: 31.

~~15.~~6. The antibody molecule of claim ~~14~~ 5 which comprises SEQ ID NO: 32, or SEQ ID NO: 33.

~~16.~~7. The antibody molecule of claim ~~13~~ 5 having a heavy chain comprising SEQ ID NO: 34 or SEQ ID NO: 40, and a light chain comprising SEQ ID NO: 35~~, or having a heavy chain comprising SEQ ID NO: 42, and a light chain comprising SEQ ID NO: 43~~.

~~17.~~8. The antibody of claim ~~13~~ 4 which is a Fab molecule having a Fd fragment comprising SEQ ID NO: 36, SEQ ID NO: 38, or SEQ ID NO: 41, and a light chain comprising SEQ ID NO: 37 or SEQ ID NO: 39.

~~18.~~9. The antibody molecule of any one of the preceding claims for use in medicine.

~~19.~~10. Antibody molecule of any one of the preceding claims for use in the therapy or prevention of side effects of anticoagulant therapy, and/or for reversal of an overdosing of an anticoagulant.

~~20.~~11. Antibody molecule of claim ~~19~~10, wherein the side effect is a bleeding event.

~~21.~~12. Method of manufacturing an antibody molecule of any one of the preceding claims, comprising

(a) providing a host cell comprising one or more nucleic acids encoding said antibody molecule in functional association with an expression control sequence,

(b) cultivating said host cell, and

(c) recovering the antibody molecule from the cell culture.

~~22.~~13. A kit comprising an antibody of any one of claims 1 to ~~20~~8, or a pharmaceutical composition thereof.

~~23.~~14. A kit comprising:

(a) an antibody of any one of claims 1 to ~~20~~8, or a pharmaceutical composition thereof;

(b) a container; and

(c) a label.

~~24.~~15. A kit comprising an antibody of any one of claim~~s~~ ~~7~~1 to ~~20~~8, and dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof.

~~25.~~16. The kit according to claim ~~24~~15, wherein the form of dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof is in the form of a solid, liquid or gel.

~~26.~~17. The kit according to claim ~~24~~15, wherein the pharmaceutically acceptable salt of dabigatran etexilate is a mesylate salt.

~~27.~~18. The kit according to claim ~~24~~15 or ~~26~~17, wherein the strength per dosage unit of the dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof is between 75 mg and 300 mg, either QD or BID.

~~28.~~19. A kit comprising:

(a) an antibody of any one of claims ~~7~~1 to ~~20~~8, or a pharmaceutical composition thereof;

(b) a pharmaceutical composition of dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof;

(c) a container; and

(d) a label.

~~29.~~ 20. The kit according to claim ~~28~~19, wherein the form of dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof is in the form of a solid, liquid or gel.

~~30.~~ 21. The kit according to claim ~~28~~19, wherein the pharmaceutically acceptable salt of dabigatran etexilate is a mesylate salt.

~~31.~~ 22. The kit according to claim ~~28~~19 or ~~30~~21, wherein the strength per dosage unit of the dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof is between 75 mg and 300 mg, either QD or BID.

~~32.~~ 23. A kit comprising:

(a) a first pharmaceutical composition comprising dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof;

(b) a second pharmaceutical composition comprising an antibody of any one of claims ~~7~~1 to ~~20~~8;

(c) instructions for separate admininstration of said first and second pharmaceutical compositions to a patient,

wherein said first and second pharmaceutical compositions are contained in separate containers and said second pharmaceutical composition is to be administered to a patient requiring neutralization or partial neutralization of dabigatran or 1-O-acylglucuronide of dabigatran.

~~33.~~ 24. An antibody of any one of claims ~~7~~1 to ~~20~~8, or a pharmaceutical composition thereof for use in neutralizing or partially neutralizing dabigatran or 1-O-acylglucuronide of dabigatran in a patient being treated with dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof.

~~34.~~ 25. A method for neutralizing or partially neutralizing dabigatran or 1-O-acylglucuronide of dabigatran in a patient comprising:

(a) confirming that a patient was being treated with dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof, and the amount that was taken by the patient;

(b) neutralizing dabigatran or 1-O-acylglucuronide in a sample taken from the patient with an antibody of any one of claims ~~7~~ 1 to ~~20~~ 8 prior to performing a clotting or coagulation test or assay wherein dabigatran or the 1-O-acylglucuronide of dabigatran would interfere with the accurate read out of the test or assay results;

(c) performing the clotting or coagulation test or assay on a sample taken from the patient to determine the level of clot formation without dabigatran or 1-O-acylglucuronide of dabigatran present; and

(d) adjusting an amount of dabigatran, dabigatran etexilate, a prodrug of dabigatran or a pharmaceutically acceptable salt thereof that is to be administered to the patient in order to achieve the appropriate balance between clot formation and degradation in a patient.

~~35.~~ 26. The method according to claims ~~33~~ 24 or ~~34~~25, wherein the amount of antibody to dabigatran or 1-O-acylglucuronide of dabigatran is in the molar ratio of between 0.1 and 100.

~~36.~~ 27. The method according to claim ~~35~~26, wherein the amount of antibody to dabigatran or 1-O-acylglucuronide of dabigatran is in the molar ratio of between 0.1 and 10.

~~37.~~ 28. The method according to claim ~~34~~25, wherein the accurate read out of the test or assay result is an accurate read out of fibrinogen levels, activated protein C resistance or related tests.