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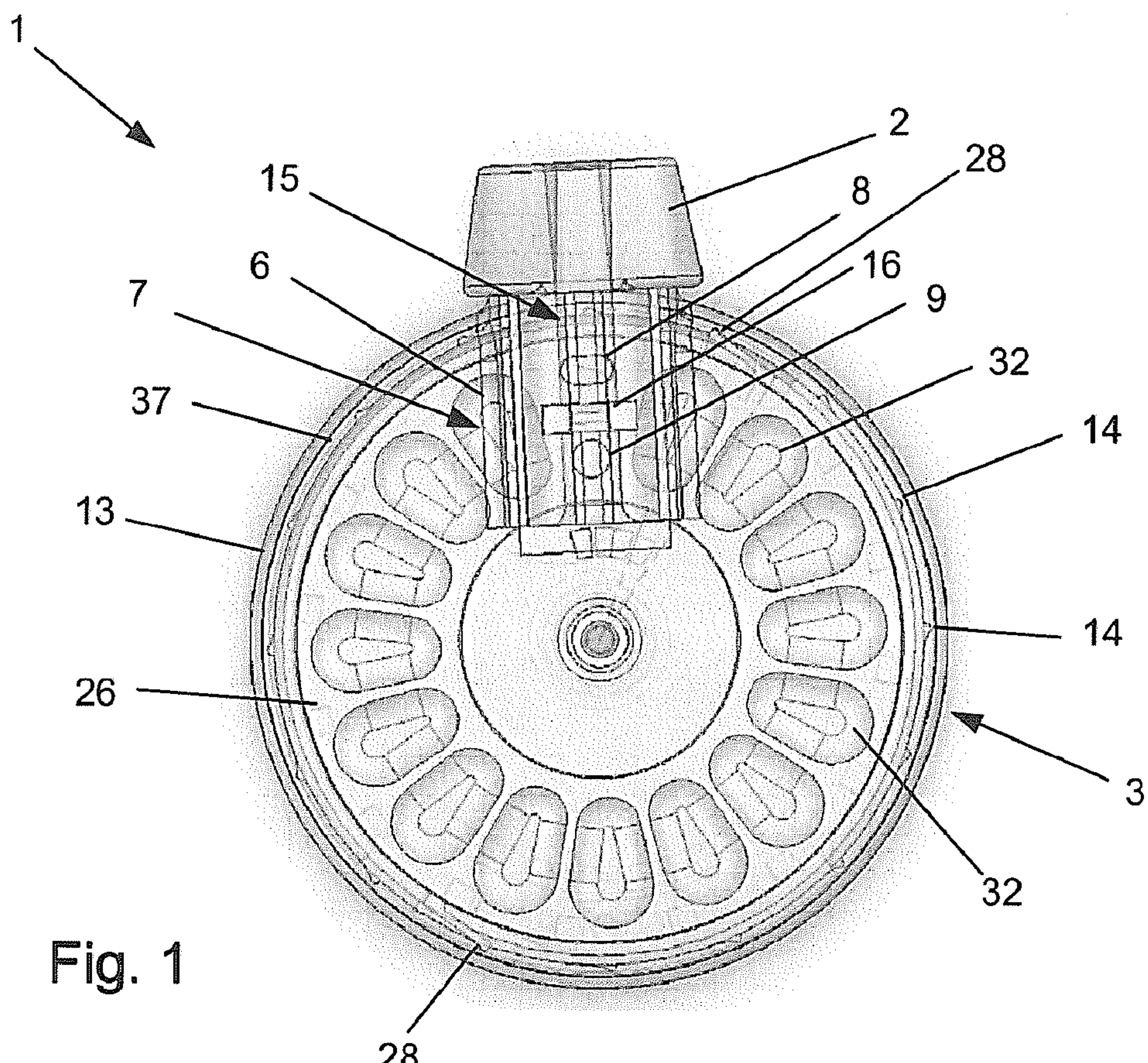
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(54) Titre : INHALATEUR

(54) Title: INHALER



(57) Abrégé/Abstract:

(57) **Abrieger/Abstract:**
An inhaler, in particular a powder inhaler, for administering a medication in the form of inhalable substances, substance formulations or mixtures, comprises a mouthpiece (2) and a magazine comprising a housing (3) with a plurality of cavities (32) for

(57) Abrégé(suite)/Abstract(continued):

holding the medication, wherein the mouthpiece (2) is in flow connection with one of the cavities (32). The closed housing (3) comprises a cover (4) covering at least one carrier (26, 27) that comprises the non-sealed cavities (32), wherein the carrier (26, 27) can be shifted relative to the cover (4) in order to bring a cavity (32) into flow connection with the mouthpiece (2).

Abstract

5 An inhaler, particularly a powder inhaler, for administering a medicament in the form of inhalable substances, substance formulations or mixtures, with a mouthpiece (2) and a magazine that comprises a housing (3) having a plurality of cavities (32) for holding the medicament, the mouthpiece (2) being in flow connection with one of the cavities (32). The closed housing (3) has a cover (4) that covers at least one carrier (26, 27)

10 comprising the unsealed cavities (32), the carrier (26, 27) being movable relative to the cover (4) for bringing a cavity (32) into flow connection with the mouthpiece (2).

15

(Fig. 1)

109409

Inhaler**Specification**

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The invention relates to an inhaler, particularly a powder inhaler, for administering a medicament in the form of inhalable substances, substance formulations or mixtures, with a mouthpiece and a magazine that comprises a housing having a plurality of 10 cavities for holding the medicament, the mouthpiece being in flow connection with one of the cavities.

Inhalers are known from the prior art in which a direct connection is made to a medicament chamber by a reduced-pressure flow produced on inhaling (venturi) and a 15 powdered medicament contained therein is removed. In an inhaler according to US-A-6 655 381 a powdered medicament is stored in an annular magazine in cavities arranged in a circle. A seal that closes off the cavities is essentially removed as a whole and a venturi tube with a constriction is arranged above the cavity parallel to the magazine. A longer turbulence chamber is connected to the venturi tube for removing the 20 medicament from the cavity essentially in one go.

In addition, there are inhalers in which a medicament chamber is opened by piercing. The openings thus formed in a sealing film are not very precisely defined, however.

25 Moreover, EP 1 844 806 A1 describes a multi-dose powder inhaler in which a drive flow is produced in an air channel and because of a constriction in the air channel produces a reduced-pressure flow in this region. The narrowest part of the air channel causing the reduced-pressure flow is connected to a discharge opening of a medicament chamber. The discharge opening is connected to a control opening, so 30 that a discharge flow is formed through the control opening via the discharge opening and through the medicament chamber. The discharge flow is not connected to the drive flow before entering the medicament chamber, but combines with the drive flow after exiting the discharge opening, as a result of which a medicament that has been

carried along with the discharge flow is transported back towards the mouthpiece with the drive flow. The medicament magazine typically comprises, in addition to the control and discharge openings, a fill opening which is provided independently of the other two openings in the magazine and which may be relatively large to make filling easier.

5 After being filled with the powder the fill opening is sealed with a film. If the medicament magazine is configured as an annular magazine with a plurality of medicament chambers arranged in a circle therein, the control and discharge opening of each chamber are spaced from one another on one side of the magazine, while the fill opening is arranged on an opposite side of the magazine.

10

The problem of the invention is to provide an inhaler of the kind mentioned hereinbefore, which is easy and reliable to operate while having a simple structure.

According to the invention the problem is solved in that the closed housing has a cover 15 that covers at least one carrier comprising the unsealed cavities, the carrier being movable relative to the cover for bringing a cavity into flow connection with the mouthpiece.

In order to use the inhaler, which is constructed in particular as a so-called multi-dose 20 powder inhaler, it is not necessary to remove a seal from the cavities or to pierce such a seal. Rather, the cavities containing the medicament are covered only by the cover of the housing. The invention is based on the finding that it is not absolutely essential to protect the medicament in the cavities from moisture by sealing with special films if the medicament is to be taken regularly and the magazine provides only as many 25 doses of medicament as are normally consumed over the life of the medicament when it is correctly stored.

Inhalers are known by the trade marks HandiHaler®, Spinhaler®, Rotahaler®, Aerolizer®, Flowcaps®, Turbospin®, AIR DPI®, Orbital®, Directhaler® and/or are described in DE 33 30 45 722, EP 0 591 136, DE 43 18 455, WO 91/02558, FR-A-2 146 202, US-A-4 069 819, EP 666085, EP 869079, US 3,991,761, WO 99/45987, WO 200051672, Bell, J. Pharm. Sci. 60, 1559 (1971); Cox, Brit. Med. J. 2, 634 (1969). Both single- and multi-dose powder inhalers are known, particularly the Spinhaler®, Rotahaler®, Aerolizer®, Inhalator®, HandiHaler®, Diskhaler®, Diskus®, Accuhaler®, Aerohaler®, Eclipse®,

Turbohaler®, Turbuhaler®, Easyhaler®, Novolizer®, Clickhaler®, Pulvinal®, Novolizer®, SkyeHaler®, Xcelovair®, Pulvina®, Taifun®, MAGhaler®, Twisthaler® and Jethaler®.

Particularly preferred in this context are medicaments selected from among the
 5 anticholinergics, betamimetics, steroids, phosphodiesterase IV inhibitors, LTD4-
 antagonists and EGFR-kinase inhibitors, antiallergics, ergot alkaloid derivatives,
 triptanes, CGRP antagonists, phosphodiesterase-V inhibitors, and combinations of
 active substances of this kind, e.g. betamimetics plus anticholinergics or betamimetics
 10 plus antiallergics. In the case of combinations at least one of the active substances
 contains chemically bound water. Anticholinergic-containing active substances are
 preferably used, as monopreparations or in the form of combined preparations.

The following are specific examples of the active ingredients or the salts thereof:

15 Anticholinergics to be used are preferably selected from among tiotropium bromide,
 oxitropium bromide, flutropium bromide, ipratropium bromide, glycopyrronium salts,
 trospium chloride, tolterodine, tropenol 2,2-diphenylpropionate methobromide, scopine
 2,2-diphenylpropionate methobromide, scopine 2-fluoro-2,2-diphenylacetate-
 methobromide, tropenol 2-fluoro-2,2-diphenylacetate-methobromide, tropenol 3,3',4,4'-
 20 tetrafluorobenzilate methobromide, scopine 3,3',4,4'-tetrafluorobenzilate
 methobromide, tropenol 4,4'-difluorobenzilate methobromide, scopine 4,4'-
 difluorobenzilate methobromide, tropenol 3,3'-difluorobenzilate methobromide, scopine
 3,3'-difluorobenzilate methobromide, tropenol 9-hydroxy-fluorene-9-carboxylate
 methobromide, tropenol 9-fluoro-fluorene-9-carboxylate methobromide, scopine 9-
 25 hydroxy-fluorene-9-carboxylate methobromide, scopine 9-fluoro-fluorene-9-carboxylate
 methobromide, tropenol 9-methyl-fluorene-9-carboxylate methobromide, scopine 9-
 methyl-fluorene-9-carboxylate methobromide, cyclopropyltropine benzilate
 methobromide, 2,2-diphenylpropionate cyclopropyltropine methobromide,
 cyclopropyltropine 9-hydroxy-xanthene-9-carboxylate methobromide,
 30 cyclopropyltropine benzilate methobromide, 2,2-diphenylpropionate cyclopropyltropine
 methobromide, cyclopropyltropine 9-hydroxy-xanthene-9-carboxylate methobromide,
 cyclopropyltropine
 9-methyl-fluorene-9-carboxylate methobromide, cyclopropyltropine 9-methyl-xanthene-
 35 9-carboxylate methobromide, cyclopropyltropine 9-hydroxy-fluorene-9-carboxylate
 methobromide, methyl cyclopropyltropine 4,4'-difluorobenzilate methobromide, tropenol

9-hydroxy-xanthene-9-carboxylate methobromide, scopine 9-hydroxy-xanthene-9-carboxylate methobromide, tropenol 9-methyl-xanthene-9-carboxylate methobromide, scopine 9-methyl-xanthene-9-carboxylate methobromide, tropenol 9-ethyl-xanthene-9-carboxylate methobromide, tropenol 9-difluoromethyl-xanthene-9-carboxylate methobromide and scopine 9-hydroxymethyl-xanthene-9-carboxylate methobromide, optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the salts, solvates and/or hydrates thereof.

Betamimetics which may be used are preferably selected from among albuterol, bambuterol, bitolterol, broxaterol, carbuterol, clenbuterol, fenoterol, formoterol, hexoprenaline, ibuterol, indacterol, isoetharine, isoprenaline, levosalbutamol, mabuterol, meluadrine, metaproterenol, orciprenaline, pirbuterol, procaterol, reproterol, rimiterol, ritodrine, salmeterol, salmefamol, soterenot, sulphonterol, tiaramide, terbutaline, tolubuterol, CHF-1035, HOKU-81, KUL-1248, 3-(4-{6-[2-hydroxy-2-(4-hydroxy-3-hydroxymethyl-phenyl)-ethylamino]-hexyloxy}-butyl)-benzenesulphonamide, 5-[2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1*H*-quinolin-2-one, 4-hydroxy-7-[2-{[2-{[3-(2-phenylethoxy)propyl]sulphonyl}ethyl]-amino}ethyl]-2(3*H*)-benzothiazolone, 1-(2-fluoro-4-hydroxyphenyl)-2-[4-(1-benzimidazolyl)-2-methyl-2-butylamino]ethanol, 1-[3-(4-methoxybenzyl-amino)-4-hydroxyphenyl]-2-[4-(1-benzimidazolyl)-2-methyl-2-butylamino]ethanol, 1-[2*H*-5-hydroxy-3-oxo-4*H*-1,4-benzoxazin-8-yl]-2-[3-(4-N,N-dimethylaminophenyl)-2-methyl-2-propylamino]ethanol, 1-[2*H*-5-hydroxy-3-oxo-4*H*-1,4-benzoxazin-8-yl]-2-[3-(4-methoxyphenyl)-2-methyl-2-propylamino]ethanol, 1-[2*H*-5-hydroxy-3-oxo-4*H*-1,4-benzoxazin-8-yl]-2-[3-(4-n-butyloxyphenyl)-2-methyl-2-propylamino]ethanol, 1-[2*H*-5-hydroxy-3-oxo-4*H*-1,4-benzoxazin-8-yl]-2-{4-[3-(4-methoxyphenyl)-1,2,4-triazol-3-yl]-2-methyl-2-butylamino}ethanol, 5-hydroxy-8-(1-hydroxy-2-isopropylaminobutyl)-2*H*-1,4-benzoxazin-3-(4*H*)-one, 1-(4-amino-3-chloro-5-trifluoromethylphenyl)-2-tert.-butylamino)ethanol and 1-(4-ethoxycarbonylamino-3-cyano-5-fluorophenyl)-2-(tert.-butylamino)ethanol, optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the pharmacologically acceptable acid addition salts, solvates and/or hydrates thereof.

Steroids which may be used are preferably selected from among prednisolone, prednisone, butixocortpropionate, RPR-106541, flunisolide, beclomethasone, triamcinolone, budesonide, fluticasone, mometasone, ciclesonide, rofleponide, ST-

126, dexamethasone, (S)-fluoromethyl 6 α ,9 α -difluoro-17 α -[(2-furanylcarbonyl)oxy]-11 β -hydroxy-16 α -methyl-3-oxo-androsta-1,4-diene-17 β -carbothionate, (S)-(2-oxo-tetrahydro-furan-3S-yl) 6 α ,9 α -difluoro-11 β -hydroxy-16 α -methyl-3-oxo-17 α -propionyloxy-androsta-1,4-diene-17 β -carbothionate and etiprednol-dichloroacetate (BNP-166), optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the salts and derivatives thereof, the solvates and/or hydrates thereof.

PDE IV inhibitors which may be used are preferably selected from among enprofyllin, theophyllin, roflumilast, ariflo (cilomilast), CP-325,366, BY343, D-4396 (Sch-351591), AWD-12-281 (GW-842470), N-(3,5-dichloro-1-oxo-pyridin-4-yl)-4-difluoromethoxy-3-cyclopropylmethoxybenzamide, NCS-613, pumafentine, (-)p-[(4aR*,10bS*)-9-ethoxy-1,2,3,4,4a,10b-hexahydro-8-methoxy-2-methylbenzo[s][1,6]naphthyridin-6-yl]-N,N-diisopropylbenzamide, (R)-(+)-1-(4-bromobenzyl)-4-[(3-cyclopentyloxy)-4-methoxyphenyl]-2-pyrrolidone, 3-(cyclopentyloxy-4-methoxyphenyl)-1-(4-N'-[N-2-cyano-S-methyl-isothioureido]benzyl)-2-pyrrolidone, cis[4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexane-1-carboxylic acid], 2-carbomethoxy-4-cyano-4-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)cyclohexan-1-one, cis[4-cyano-4-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)cyclohexan-1-ol], (R)-(+)-ethyl[4-(3-cyclopentyloxy-4-methoxyphenyl)pyrrolidin-2-ylidene]acetate, (S)-(-)-ethyl[4-(3-cyclopentyloxy-4-methoxyphenyl)pyrrolidin-2-ylidene]acetate, CDP840, Bay-198004, D-4418, PD-168787, T-440, T-2585, arofyllin, atizoram, V-11294A, CI-1018, CDC-801, CDC-3052, D-22888, YM-58997, Z-15370, 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-a]pyridine and 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(tert-butyl)-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-a]pyridine, optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the pharmacologically acceptable acid addition salts, solvates and/or hydrates thereof.

LTD4-antagonists which may be used are preferably selected from among montelukast, 1-(((R)-(3-(2-(6,7-difluoro-2-quinolinyl)ethenyl)phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio)methylcyclopropane-acetic acid, 1-(((1(R)-3(3-(2-(2,3-dichlorothieno[3,2-b]pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)propyl)thio)-methyl)cyclopropane-acetic acid, pranlukast, zafirlukast, [2-[[2-(4-tert-butyl-2-thiazolyl)-5-benzofuranyl]oxymethyl]phenyl]acetic acid,

MCC-847 (ZD-3523), MN-001, MEN-91507 (LM-1507), VUF-5078, VUF-K-8707 and L-733321, optionally in the form of the racemates, enantiomers or diastereomers thereof, optionally in the form of the pharmacologically acceptable acid addition salts thereof and optionally in the form of the salts and derivatives thereof, the solvates and/or 5 hydrates thereof.

EGFR-kinase inhibitors which may be used are preferably selected from among cetuximab, trastuzumab, ABX-EGF, Mab ICR-62, 4-[(3-chloro-4-fluorophenyl)amino]-6-{{4-(morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-7-cyclopropylmethoxy-quinazoline, 4-[(R)-(1-phenyl-ethyl)amino]-6-{{4-(morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-7-cyclopentyloxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{{4-((R)-6-methyl-2-oxo-morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-7-[(S)-(tetrahydrofuran-3-yl)oxy]-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[2-((S)-6-methyl-2-oxo-morpholin-4-yl)-ethoxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluorophenyl)amino]-6-{{4-[N-(2-methoxy-ethyl)-N-methyl-amino]-1-oxo-2-buten-1-yl]amino}-7-cyclopropylmethoxy-quinazoline, 4-[(R)-(1-phenyl-ethyl)amino]-6-{{4-[N-(tetrahydropyran-4-yl)-N-methyl-amino]-1-oxo-2-buten-1-yl]amino}-7-cyclopropylmethoxy-quinazoline, 4-[(3-chloro-4-fluorophenyl)amino]-6-{{4-[N-(2-methoxy-ethyl)-N-methyl-amino]-1-oxo-2-buten-1-yl]amino}-7-cyclopentyloxy-quinazoline, 4-[(3-chloro-4-fluorophenyl)amino]-6-{{4-(N,N-dimethylamino)-1-oxo-2-buten-1-yl]amino}-7-ethoxy-quinoline, 4-[(R)-(1-phenyl-ethyl)amino]-6-(4-hydroxy-phenyl)-7H-pyrrolo[2,3-d]pyrimidine, 3-cyano-4-[(3-chloro-4-fluorophenyl)amino]-6-{{4-(N,N-dimethylamino)-1-oxo-2-buten-1-yl]amino}-7-ethoxy-quinoline, 4-[(R)-(1-phenyl-ethyl)amino]-6-{{4-((R)-6-methyl-2-oxo-morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluorophenyl)amino]-6-{{4-(morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-7-[(tetrahydrofuran-2-yl)methoxy]-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-{{4-(5,5-dimethyl-2-oxo-morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{2-[4-(2-oxo-morpholin-4-yl)-piperidin-1-yl]-ethoxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-amino-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-methanesulphonylamino-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(tetrahydropyran-3-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[(morpholin-4-yl)carbonyl]-piperidin-4-yloxy}-7-methoxy- 10 15 20 25 30

quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(piperidin-3-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[1-(2-acetyl-amino-ethyl)-piperidin-4-yloxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(tetrahydropyran-4-yloxy)-7-ethoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{trans-4-[(morpholin-4-yl)carbonyl-amino]-cyclohexan-1-yloxy}-7-methoxy-quinazoline,

5 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[(piperidin-1-yl)carbonyl]-piperidin-4-yloxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(cis-4-{N-[(morpholin-4-yl)carbonyl]-N-methyl-amino}-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-ethanesulphonyl-amino-cyclohexan-1-yloxy)-7-

10 10 methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-methanesulphonyl-piperidin-4-yloxy)-7-(2-methoxy-ethoxy)-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[1-(2-methoxy-acetyl)-piperidin-4-yloxy]-7-(2-methoxy-ethoxy)-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-(tetrahydropyran-4-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(cis-4-{N-[(piperidin-1-yl)carbonyl]-N-15 methyl-amino}-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{cis-4-[(morpholin-4-yl)carbonyl-amino]-cyclohexan-1-yloxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[2-(2-oxopyrrolidin-1-yl)ethyl]-piperidin-4-yloxy}-7-methoxy-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-(1-acetyl-piperidin-4-yloxy)-7-methoxy-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-(1-

20 20 methyl-piperidin-4-yloxy)-7-methoxy-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-(1-methanesulphonyl-piperidin-4-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-methyl-piperidin-4-yloxy)-7-(2-methoxy-ethoxy)-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-{1-[(morpholin-4-yl)carbonyl]-piperidin-4-yloxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[(N-methyl-N-2-methoxyethyl-amino)carbonyl]-piperidin-4-yloxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-ethyl-piperidin-4-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[cis-4-(N-methanesulphonyl-N-methyl-amino)-cyclohexan-1-yloxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[cis-4-(N-acetyl-N-25 methyl-amino)-cyclohexan-1-yloxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-methyl-amino-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[trans-4-(N-methanesulphonyl-N-methyl-amino)-cyclohexan-1-yloxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-dimethyl-amino-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-{N-[(morpholin-4-yl)carbonyl]-N-methyl-amino}-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[2-

30 30 35

(2,2-dimethyl-6-oxo-morpholin-4-yl)-ethoxy]-7-[(S)-(tetrahydrofuran-2-yl)methoxy]-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-methanesulphonyl-piperidin-4-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-cyano-piperidin-4-yloxy)-7-methoxy-quinazoline, and 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[(2-methoxyethyl)carbonyl]-piperidin-4-yloxy}-7-methoxy-quinazoline, optionally in the form of the racemates, enantiomers or diastereomers thereof, optionally in the form of the pharmacologically acceptable acid addition salts thereof, the solvates and/or hydrates thereof.

10 By acid addition salts with pharmacologically acceptable acids which the compounds may be capable of forming are meant, for example, salts selected from among the hydrochloride, hydrobromide, hydriodide, hydrosulphate, hydrophosphate, hydromethanesulphonate, hydronitrate, hydromaleate, hydroacetate, hydrobenzoate, hydrocitrate, hydrofumarate, hydrotartrate, hydroxalate, hydrosuccinate, hydrobenzoate
15 and hydro-p-toluenesulphonate, preferably the hydrochloride, hydrobromide, hydrosulphate, hydrophosphate, hydrofumarate and hydromethanesulphonate.

Examples of antiallergics are: disodium cromoglycate, nedocromil.

20 Examples of ergot alkaloids are: dihydroergotamine, ergotamine.

Examples of substances suitable for inhalation include medicaments containing the above-mentioned active substances, and the salts and esters thereof and combinations of these active substances, salts and esters.

25 Preferably the plastics from which individual parts of the inhaler are produced are polymers, thermoplastic polycondensates, polyadducts, modified natural substances or rubbers or mixtures of these plastics.

30 Particularly preferred in this case are polyolefins, vinyl chloride polymers, styrene polymers, polyacetals, polyamides, thermoplastic polyesters and polyarylethers or mixtures of these plastics. Examples of these plastics are polyethylene, polyvinyl chloride, polyoxymethylene, polyacetal, acrylonitrile/butadiene/styrene (ABS), acrylonitrile/styrene/acrylic ester (ASA), polyamides, polycarbonate,
35 poly(ethyleneterephthalate), poly(butyleneterephthalate) or poly(phenylene ether).

Plastics of this kind may be obtained for example from the company Ensinger in Nufringen, Germany.

According to one feature the cover comprises an exit opening and an entry opening, 5 which are arranged at a spacing from each other in the region of the mouthpiece, while at least the exit opening is arranged in the region of the dish-shaped cavity that is to be emptied. Accordingly, the flow channel is configured so that at least some of the discharge flow produced on inhaling flows out over the medicament contained in the cavity and carries it along. The break-up and dispersion of the medicament can be 10 influenced by an internal configuration of the cavity and/or the exit or entry opening and/or the mouthpiece.

Expediently, the mouthpiece which is open at both ends has a cross-sectional constriction between the in particular slot-shaped exit opening and the entry opening. 15 Starting from an open entry end remote from the user of the inhaler, the air sucked in during inhalation flows through both the cross-sectional constriction and the entry opening into the cavity and, laden with medicament, flows through the exit opening to the exit end of the mouthpiece. The cross-sectional constriction improves the break-up and dispersion of the medicament in the mouthpiece by means of turbulence.

20 Preferably, the mouthpiece is held, more particularly releasably, in a defined position in a receptacle in the form of a T-shaped groove in the cover. The T-groove-shaped receptacle assists with the mounting of the mouthpiece or its attachment to the cover during the manufacture of the inhaler. If the mouthpiece is releasably attached to the 25 cover it can be removed from the magazine for cleaning. It is also possible to replace only the magazine if necessary and to continue using the mouthpiece.

According to a further feature the housing comprises a base to which the cover is non-removably attached in sealed manner. If both the cover and the base are made of a 30 plastics material, they may be joined together by welding, for example. Naturally, the carrier is protected by being held between the cover and the base.

Preferably, the housing has a circular cross-section and provides a latching rotatable mounting for the disc-shaped carrier, while an actuating device for stepwise rotation of

the carrier is associated with the housing and the carrier so as to move a cavity that is to be emptied into the flow channel with the mouthpiece. Using the actuating device the user can move the carrier so that a cavity filled with the medicament moves into the flow channel, i.e. underneath the exit opening at the cover end, and assumes a defined 5 position therein. Thus the inhaler is easy and reliable to operate.

According to a further feature, two disc-shaped carriers are rotatably mounted in locking manner in the housing, so as to be rotatably located directly above one another, while the carrier associated with the mouthpiece comprises an exit opening 10 and an entry opening which correspond to the outlet opening and inlet opening of the cover. In this way a plurality of doses of a medicament to be administered can be stored in a magazine of compact construction. The medicament from the carrier on the base side passes through the exit opening in the carrier on the mouthpiece side and the exit opening in the cover into the mouthpiece. At the same time, the air sucked in 15 is guided through the entry opening of the cover and the inlet opening of the carrier on the mouthpiece side to the cavity, the two carriers naturally being located with their facing end faces directly against one another so as to prevent loss of flow and loss of medicament.

20 In order to provide a mount of simple construction, the carrier facing the mouthpiece comprises a circumferential flange with an external diameter greater than that of the carriers, in which on the one hand the carrier on the base side is mounted with its end face comprising the cavities and on the other hand is supported in the housing. It goes without saying that an additional spindle may pass through the entire housing of the 25 magazine with its carriers to ensure accurate guidance.

Advantageously, the actuating device comprises an actuating element that is mounted 30 in the base so as to be movable along a circular path, this actuating element engaging via a spring arm in equidistant recesses in the carrier on the base side, and the two carriers have tappets that move into mutual abutment when the carrier on the base side is rotated by one revolution out of a starting position. This provides an actuating device of simple construction for reliably rotating the two carriers in the housing.

In order to achieve precise positioning, for stepwise rotation of the two carriers at least one spring arm cooperating with the circumference of the pot-shaped cover is expediently associated with each carrier. In particular, two diametrically opposed 5 spring arms are provided on each carrier, while the carriers may for example be manufactured in one piece with the spring arms by an injection moulding process.

For further improving the handling of the inhaler and for ensuring the efficacy of the medicament, a desiccant and/or a, more particularly, digital moisture indicator is or are 10 provided inside the housing. Of course, the desiccant, which has no negative effects on the medicament stored in the magazine of the inhaler, can be accommodated in a special chamber. The moisture indicator provides information as to the relative humidity within the housing, which is visually apparent to the user, by means of which it is possible to determine whether or not the medicament can be used, for example. A 15 digital moisture indicator may comprise changing colours, particularly green and red, or a written warning notice.

In order to obtain the most uniform possible distribution of the pharmaceutical powder formulation, the mouthpiece is fitted with a dispersing unit.

20 Expediently, each cavity is designed to hold about 50 mg of the medicament and the magazine preferably comprises 30 cavities. The cavities are distributed equidistantly over the circumference of the carrier, including a blank position which comprises the outlet opening and the inlet opening on the carrier on the cover side, each carrier 25 having 15 cavities. Theoretically, any other number of cavities is also possible, for example four, six, eight, ten, twelve, 16, 20, 24 or 32.

For monitoring the contents of different cavities in the magazine of the inhaler, the housing is constructed to be at least partly transparent, to enable a visual check to be 30 made through this transparent section as to whether one or more cavities have already been emptied or are still full. For example, the transparent section is arranged such that it is always possible to see into the particular cavity that will be accessed next through the mouthpiece, i.e. the one in front of a dispensing or inhaling position, viewed in the direction of rotation of the carriers.

To protect the medicament in the cavities of the carriers of the magazine from moisture over relatively long periods, a removable moistureproof outer wrapper for the inhaler and/or the magazine is provided.

5

It will be understood that the features mentioned above and still to be explained hereinafter may be used not only in the particular combination stated but also in other combinations. The scope of the invention is defined only by the claims.

10 The invention is hereinafter explained in more detail by means of an embodiment by way of example with reference to the accompanying drawings, wherein:

Figure 1 is a plan view of an inhaler according to the invention,

15 Figure 2 is a side view of the inhaler according to Figure 1,

Figure 3 is a plan view of a mouthpiece of the inhaler according to Figure 1,

20 Figure 4 is a sectional view of the mouthpiece along the line IV-IV in Figure 3,
Figure 5 is a plan view of a restrictor for the mouthpiece according to Figure 3,

Figure 6 is a plan view of a cover of the inhaler according to Figure 1,

25 Figure 7 is a sectional view of the cover on the line VII-VII in Figure 6,

Figure 8 is a plan view of a base of the inhaler according to Figure 1,

30 Figure 9 is a sectional view of an actuator of the inhaler according to Figure 1,
Figure 10 is a plan view of an actuating element of the inhaler according to

Figure 1,

Figure 11 is a side view of the actuating element according to Figure 10,

Figure 12 is a plan view of a carrier of the inhaler according to Figure 1,

5 Figure 13 is a sectional view of the carrier on the line XIII-XIII according to
Figure 12,

Figure 14 is a plan view of another carrier of the inhaler according to Figure 1
and

10 Figure 15 is a sectional view of the carrier on the line XV-XV in Figure 14.

The inhaler 1 is configured as a so-called multi-dose powder inhaler for administering a powdered medicament in the form of an inhalable substance, substance formulation or mixture, and comprises a mouthpiece 2 that is connected to a housing 3 of a magazine 15 for holding a plurality of doses of the medicament. The housing 3 consists essentially of a cover 4 and a base 5 fixedly attached thereto, the cover 4 having two legs 6 to form a receptacle 7 in the form of a T-shaped groove for the mouthpiece 2. Between the two legs 6, a slot-shaped exit opening 8 and an entry opening 9 for an airflow are provided in the cover 4 at a spacing from one another. In the region of the exit 8 and 20 entry opening 9 a raised sealing surface 10 on which the mouthpiece 2 partially rests is formed on the cover 4. In the centre of the cover 4 is a bore 11 for accommodating a spindle passing through the housing 3. The cover 3 is substantially pot-shaped while an attachment 13 for centring the base 5 and equidistantly distributed indentations 14 are formed on the circumferential wall 12.

25 The mouthpiece 2 has a channel 15 extending through its longitudinal axis, in which is inserted a restrictor 16 that reduces the cross-section of the channel 15. Perpendicularly to the longitudinal axis of the mouthpiece 2 a recess 17 is formed in the mouthpiece 2, into which the restrictor 16 is inserted such that it is located in the 30 position of the mouthpiece 2 mounted on the cover 4 between the exit 8 and entry opening 9 of the cover 4 and forms a flow channel through a depression 18 in the restrictor 16. The part of the mouthpiece 2 that is to be secured has legs 19 on both sides for insertion in the T-groove-shaped receptacle 7 in the cover 4.

The base 5 is provided with an opening 20 in the shape of a segment of a circle, through which an actuator 23 connected by bolts 22 to an equally segment-shaped actuating element 21 projects, the actuating element 21 comprising a spring arm 24 projecting into the housing 3. Moreover, a chamber 25 for a desiccant is formed on the 5 base 5.

Rotatably mounted in the housing 3 of circular cross-section are two circular carriers 26, 27 arranged immediately above one another, on which two diametrically opposed spring arms 28 are arranged which cooperate for stepwise positioning of the carriers 10 26, 27 with the circumferential indentations 14 of the pot-shaped cover 4. Moreover, each carrier 26, 27 comprises a tappet 29 which can cooperate with the tappet 29 of the other carrier 26, 27 in each case.

The carrier 27 on the base side comprises, on its end face 30 facing the base 5, 15 equidistantly distributed recesses in which the spring arm 24 of the actuating element 21 engages. Moreover, including a blank position 31, dish-shaped cavities 32 for holding the medicament are uniformly distributed around the circumference of the carrier 27.

20 The cavities 32 uniformly distributed around the circumference of the carrier 26 are also formed on the end face 33 facing the cover 4, in the carrier 26 on the cover side, while in one position 34, instead of a cavity 32, an outlet opening 35 and an inlet opening 36 are provided which correspond to the exit opening 8 and the entry opening 9 of the cover 4, the outlet opening 35 and the exit opening 8 each being slot-shaped 25 and the inlet opening 36 and the entry opening 9 each being cylindrical in shape. Furthermore, the carrier 26 facing the mouthpiece 2 has a circumferential flange 37 that is larger in its external diameter than the carriers 26, 27, in which on the one hand the carrier 27 on the base side is mounted with its end face 38 comprising the cavities 32, and on the other hand is supported in the cover 4 of the housing 3.

30

In an initial state of the inhaler 1 in which all the cavities 32 are filled with the medicament, the outlet opening 35 and the inlet opening 36 of the carrier 26 on the cover side are in a position that is flush with the exit opening 8 and the entry opening 9 of the cover 4, and the blank position 31 of the carrier 27 on the base side is aligned

with the exit opening 8 and the entry opening 9 underneath the position 34 of the carrier 26 on the cover side. As the cover 4 rests directly on the associated end face 33 of the carrier 26 on the cover side and the carrier 26 on the cover side rests directly at its end face on the carrier 27 on the base side, no medicament is able to escape 5 from the cavities 32.

In order to use the inhaler, the actuating element 21 is moved along with the actuator 23, the spring arm 24 of the actuating element 21 engaging in one of the recesses of the carrier 27 on the base side and rotating said carrier 27 until the spring arms 28 10 latch in the corresponding indentations 14 in the cover 4, so as to position the cavity 32 that is associated with the rotational position under the outlet opening 35 and the inlet opening 36 of the carrier 26 on the cover side. The user sucks air through the channel 15 of the mouthpiece 2, which is passed through both the restrictor 16 and the entry opening 8 of the cover 4 and the inlet opening 35 of the carrier 26 on the mouthpiece 15 side to the cavity 32 that is to be emptied, in order to convey the medicament through the outlet opening 35 of the carrier 26 on the cover side, the exit opening 8 of the cover 4 and the channel 15 of the mouthpiece 2 to the user. In this position in which the emptied cavity 32 is aligned underneath the outlet opening 35 and the inlet opening 36 of the carrier 26 on the cover side, the inhaler 1 can be transported. Moving the 20 actuator 24 back and forth rotates the carrier 27 on the base side in order to position the next cavity 32 under the outlet opening 35 and the inlet opening 36 of the carrier 26 on the cover side. Once all the cavities 32 of the carrier 27 on the base side have been emptied, the two tappets 29 move into mutual engagement and a rotary movement of the carrier 27 on the base side is accompanied by a rotary movement of the carrier 26 25 on the cover side, in order to arrange the cavities 32 therein underneath the exit opening 8 and the entry opening 9 of the cover 4 for emptying, while when the two carriers 26, 27 are rotated for accurately positioning the wells 32 all the spring arms 28 are operational.

List of reference numerals

1. inhaler	32. cavity
2. mouthpiece	33. end face of 26
3. housing	34. position
4. cover	35. outlet opening
5. base	36. inlet opening
6. leg of 7	37. flange
7. receptacle	38. end face of 27
8. exit opening	
9. entry opening	
10. sealing surface	
11. bore	
12. wall of 4	
13. attachment	
14. indentation	
15. channel	
16. restrictor	
17. recess	
18. depression of 16	
19. leg of 2	
20. opening	
21. actuating element	
22. bolt	
23. actuator	
24. spring arm	
25. chamber	
26. carrier	
27. carrier	
28. spring arm of 26, 27	
29. tappet	
30. end face of 27	
31. blank position	

Patent Claims

5 1. Inhaler, particularly a powder inhaler, for administering a medicament in the
form of inhalable substances, substance formulations or mixtures, with a
mouthpiece (2) and a magazine that comprises a housing (3) having a plurality
of cavities (32) for holding the medicament, the mouthpiece (2) being in flow
connection with one of the cavities (32), **characterised in that** the closed
10 housing (3) has a cover (4) that covers at least one carrier (26, 27) comprising
the unsealed cavities (32), the carrier (26, 27) being movable relative to the
cover (4) for bringing a cavity (32) into flow connection with the mouthpiece (2).

15 2. Inhaler according to claim 1, **characterised in that** the cover (4) comprises an
exit opening (8) and an entry opening (9), which are arranged at a spacing from
each other in the region of the mouthpiece (2), while at least the exit opening
(8) is arranged in the region of the cup-shaped cavity (32) that is to be emptied.

20 3. Inhaler according to claim 1 or 2, **characterised in that** the mouthpiece (2)
which is open at both ends has a cross-sectional constriction between the in
particular slot-shaped exit opening (8) and the entry opening (9).

25 4. Inhaler according to one of claims 1 to 3, **characterised in that** the mouthpiece
(2) is held, more particularly releasably, in a defined position in a receptacle (7)
in the form of a T-shaped groove in the cover (4).

30 5. Inhaler according to one of claims 1 to 4, **characterised in that** the housing (3)
comprises a base (5) to which the cover (4) is non-removably attached in
sealed manner.

6. Inhaler according to one of claims 1 to 5, **characterised in that** the housing (3)
has a circular cross-section and provides a latching rotatable mounting for the
disc-shaped carrier (26, 27), while an actuating device for stepwise rotation of
the carrier (26, 27) is associated with the housing (3) and the carrier (26, 27) so

as to move a cavity (32) that is to be emptied into the flow channel with the mouthpiece (2).

7. Inhaler according to one of claims 1 to 6, **characterised in that** two disc-shaped carriers (26, 27) are rotatably mounted in locking manner in the housing (3), so as to be rotatably located directly above one another, while the carrier (26) associated with the mouthpiece (2) comprises an outlet opening (35) and an inlet opening (36) which correspond to the exit opening (8) and entry opening (9) of the cover (4).
10
8. Inhaler according to claim 7, **characterised in that** the carrier (26) facing the mouthpiece (2) comprises a circumferential flange (37) with an external diameter greater than that of the carriers (26, 27), in which on the one hand the carrier (27) on the base side is mounted with its end face (38) comprising the cavities (32) and on the other hand is supported in the housing (3).
15
9. Inhaler according to one of claims 6 to 8, **characterised in that** the actuating device comprises an actuating element (21) that is mounted in the base (5) so as to be movable along a circular path, this actuating element engaging via a spring arm (24) in equidistant recesses in the carrier (27) on the base side, and the two carriers (26, 27) have tappets (29) that move into mutual abutment when the carrier (27) on the base side is rotated through one revolution out of a starting position.
20
10. Inhaler according to one of claims 1 to 9, **characterised in that**, for stepwise rotation of the two carriers (26, 27), at least one spring arm (28) cooperating with the circumference of the pot-shaped cover (4) is associated with each carrier (26, 27).
25
11. Inhaler according to one of claims 1 to 10, **characterised in that** a desiccant and/or a, more particularly, digital moisture indicator is or are provided inside the housing (3).
30

12. Inhaler according to one of claims 1 to 11, **characterised in that** the mouthpiece (2) is fitted with a dispersing unit.
13. Inhaler according to one of claims 1 to 12, **characterised in that** each cavity (32) is designed to hold about 50 mg of a pharmaceutical powdered formulation and the magazine preferably comprises 30 cavities (32).
14. Inhaler according to one of claims 1 to 13, **characterised in that** the housing (3) is constructed to be at least partly transparent.
15. Inhaler according to one of claims 1 to 14, **characterised by** a removable moistureproof outer wrapper and/or an outer wrapper for the magazine.

Application number / numéro de demande: EP2009065949

Figures: 1-2

Pages: _____

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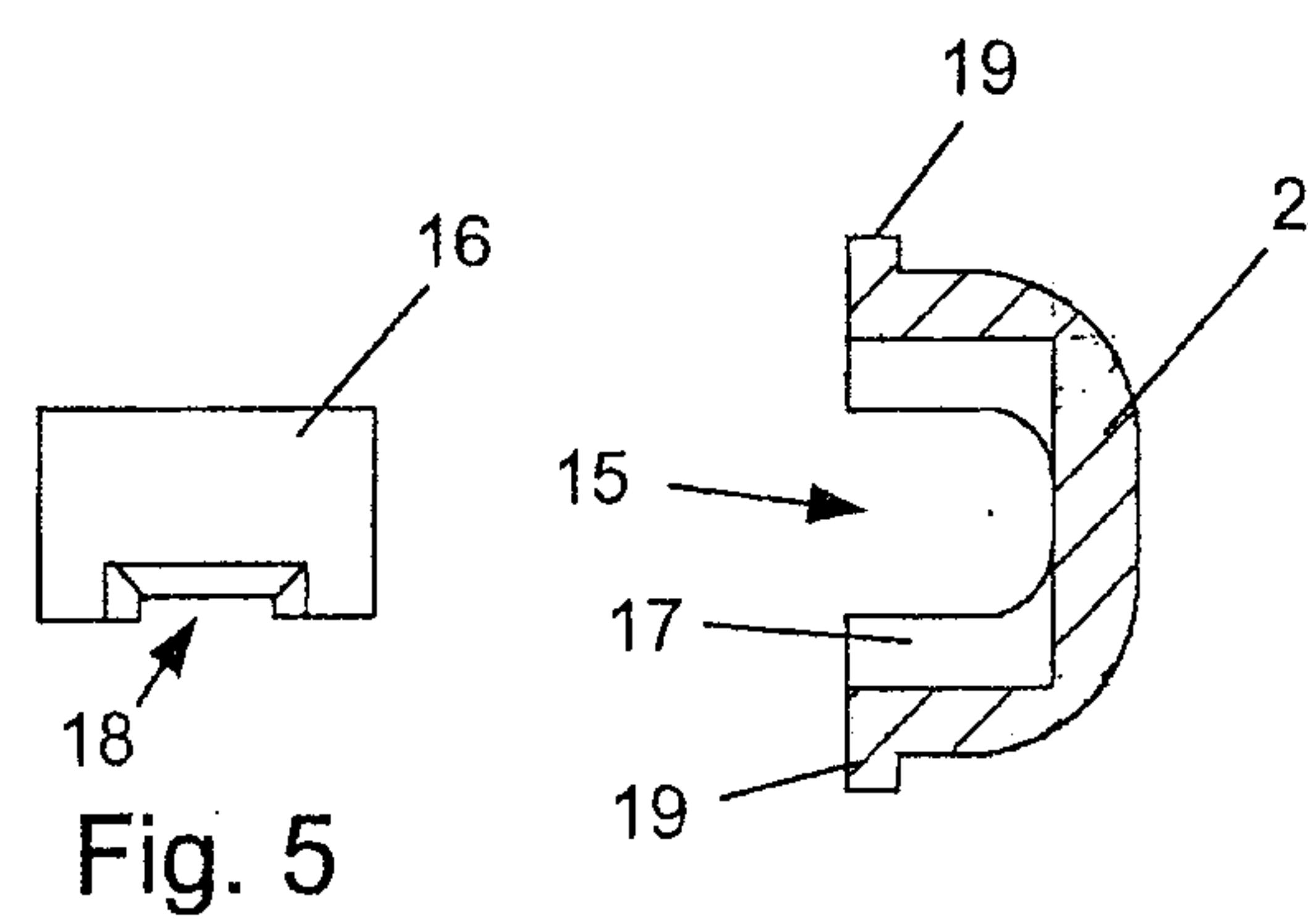
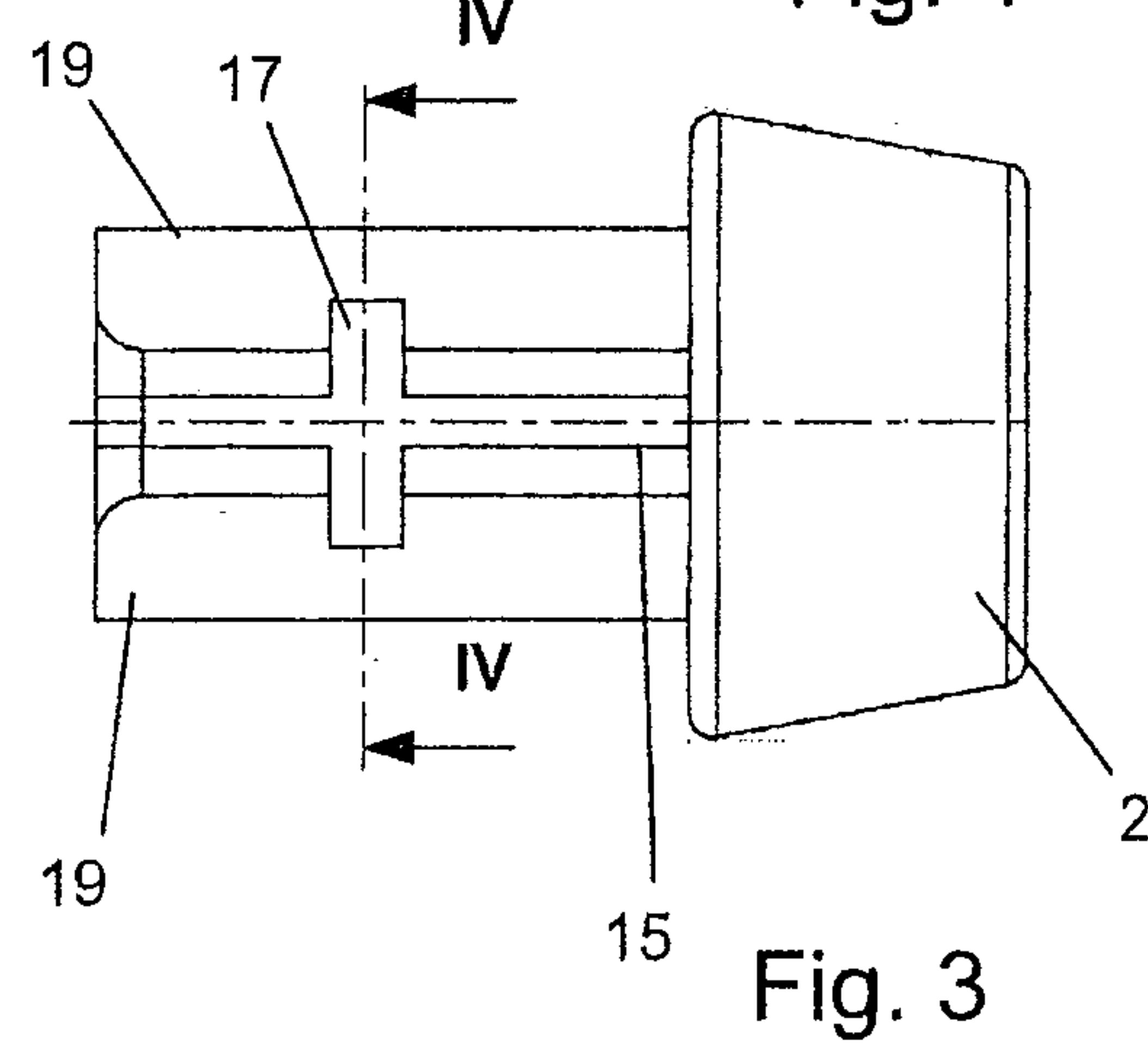


Fig. 5

Fig. 4



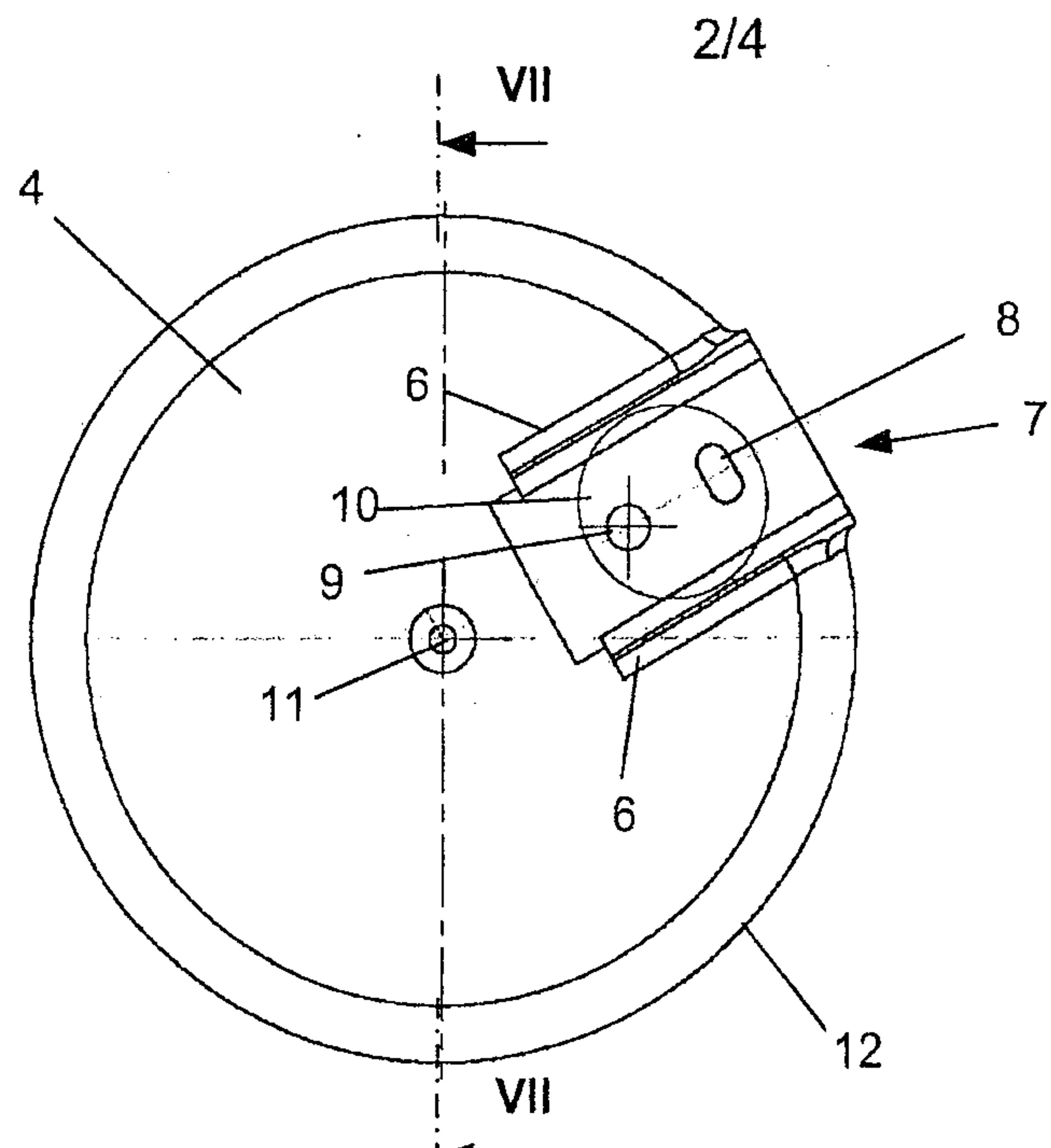


Fig. 6

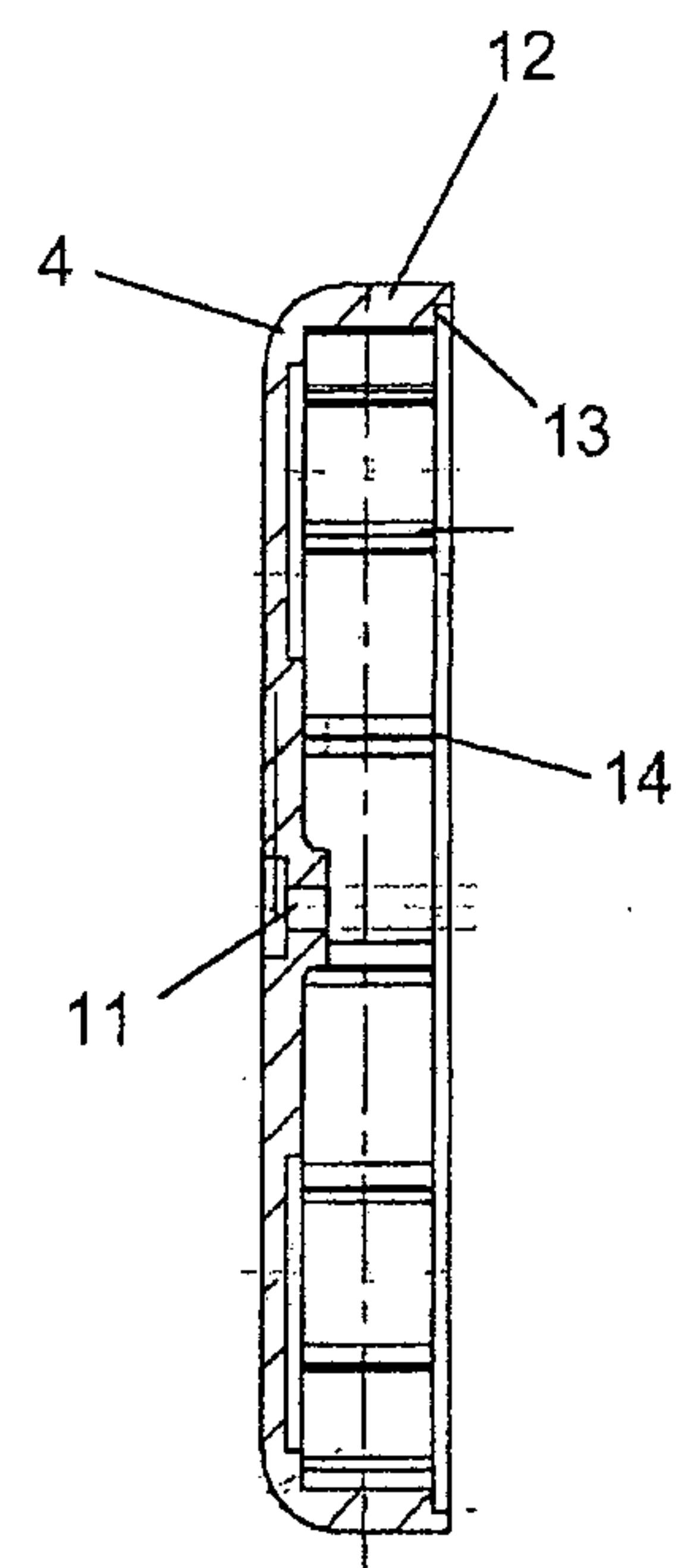


Fig. 7

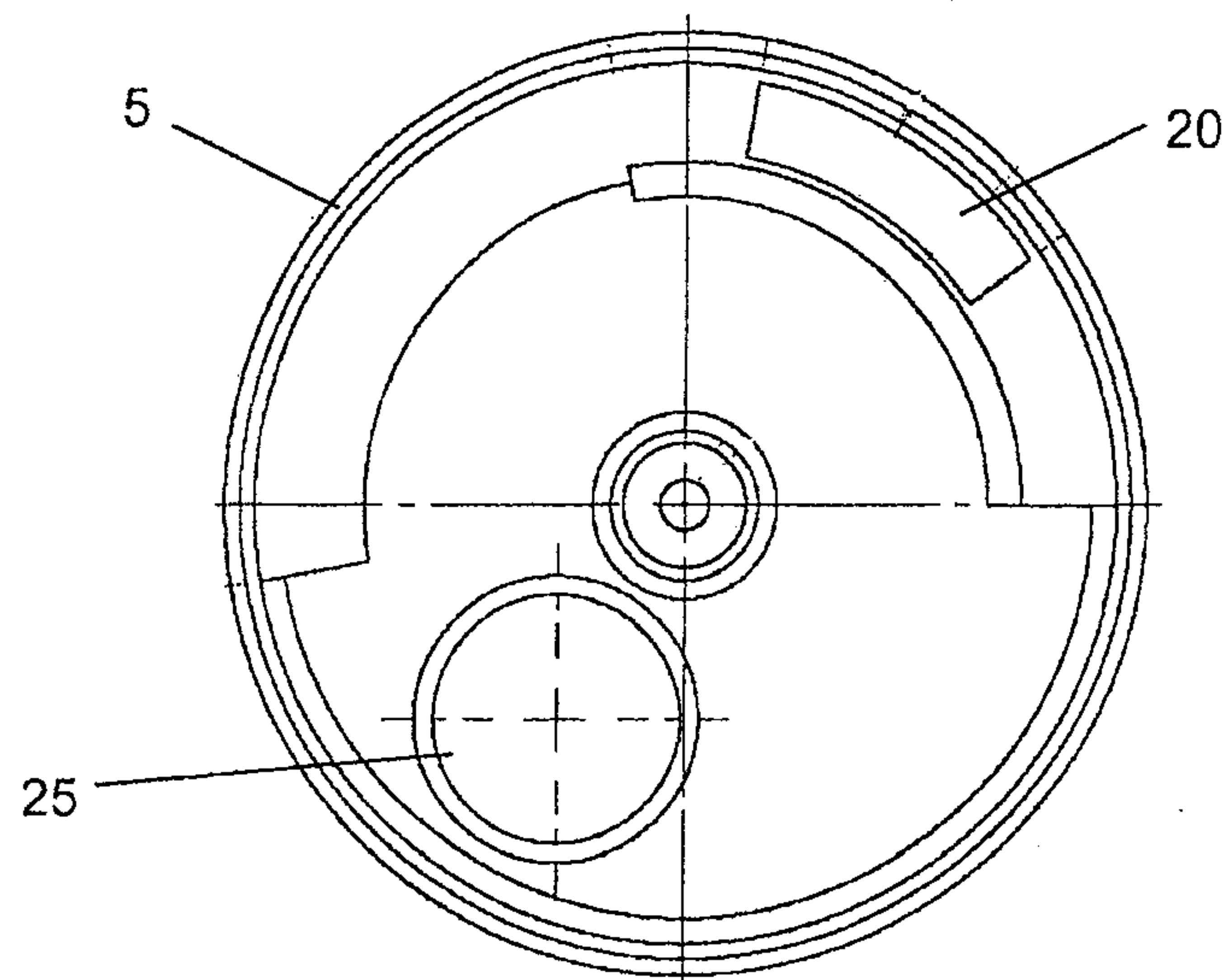


Fig. 8

3/4

Fig. 9

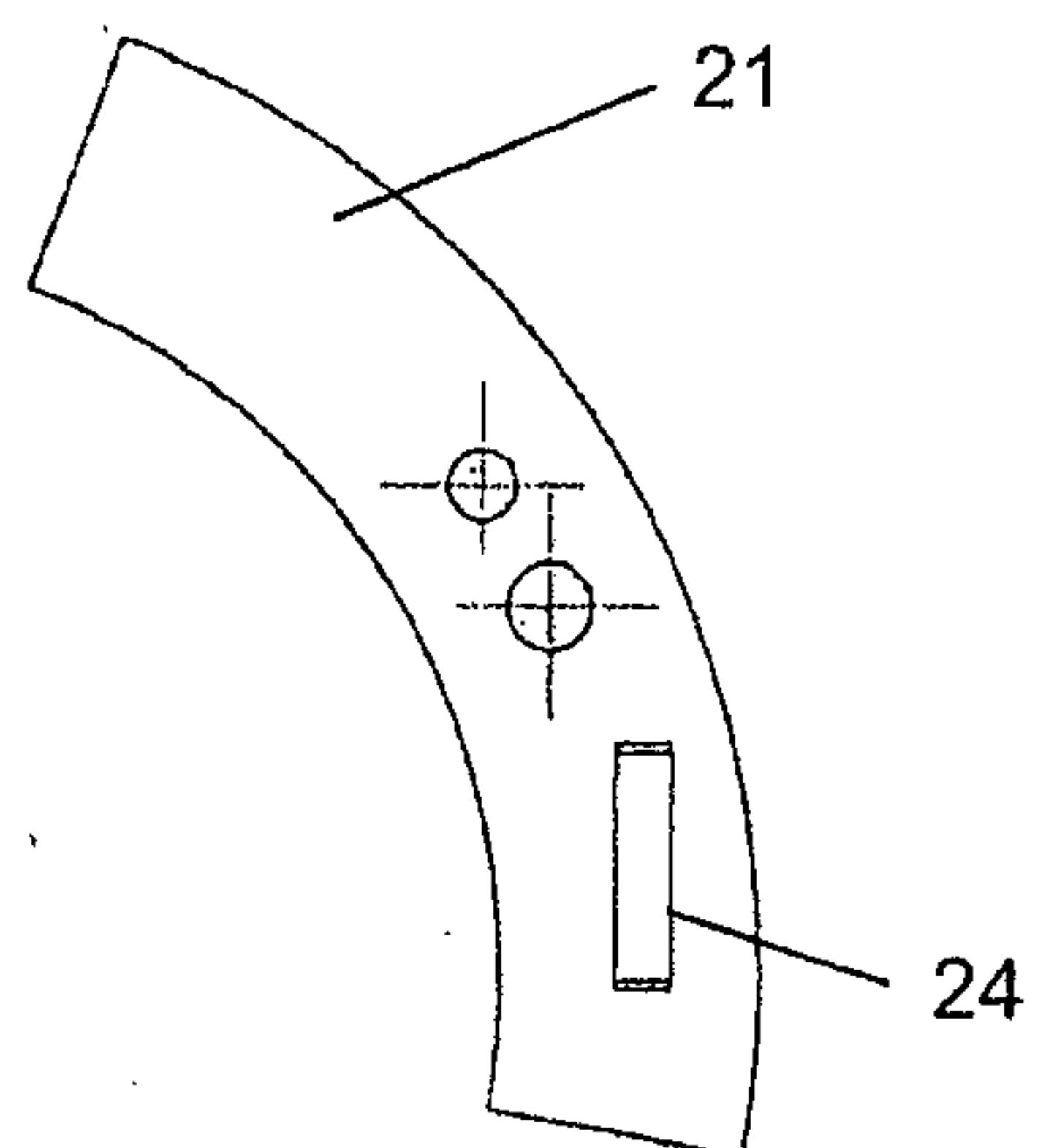
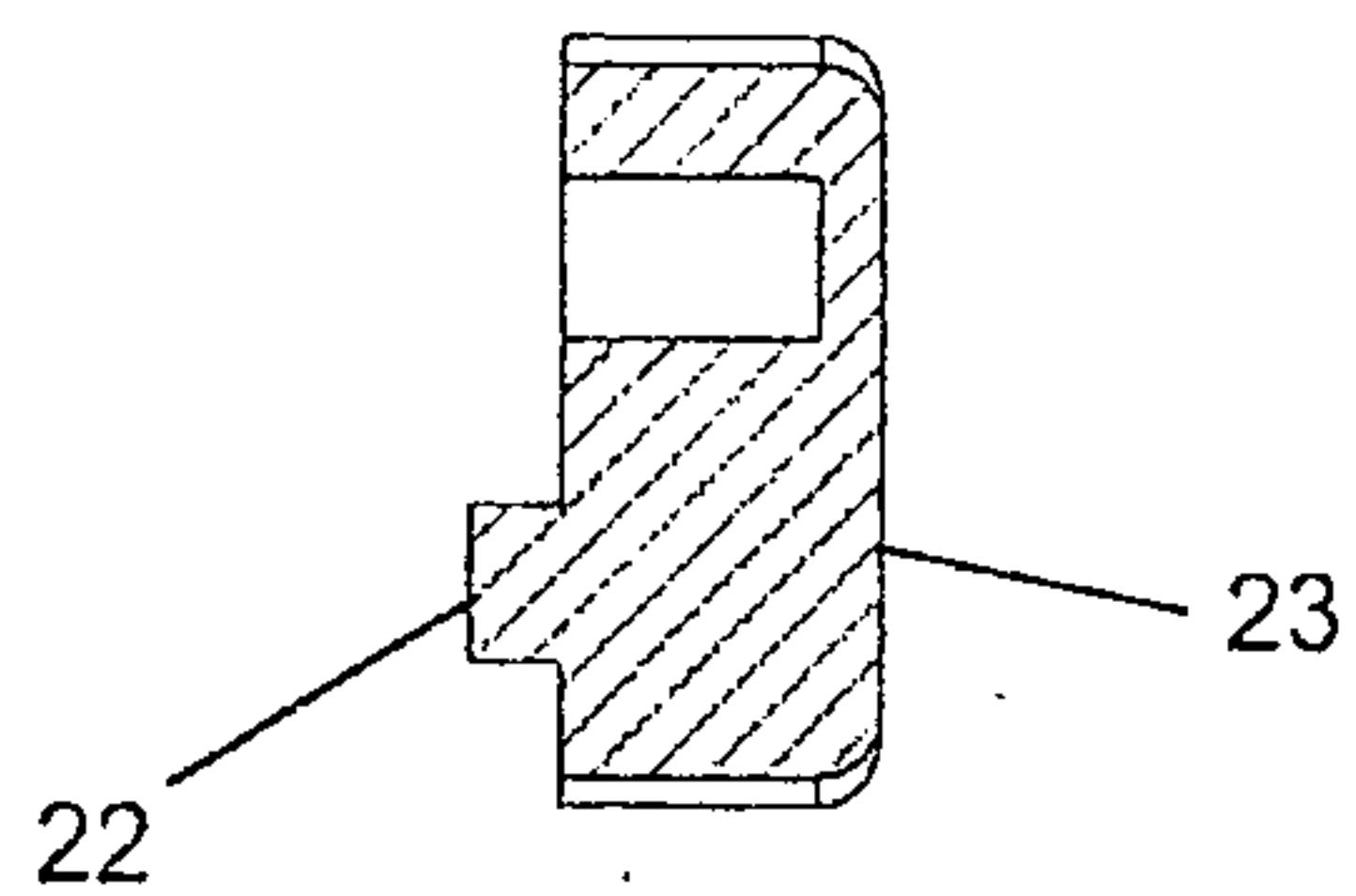


Fig. 10

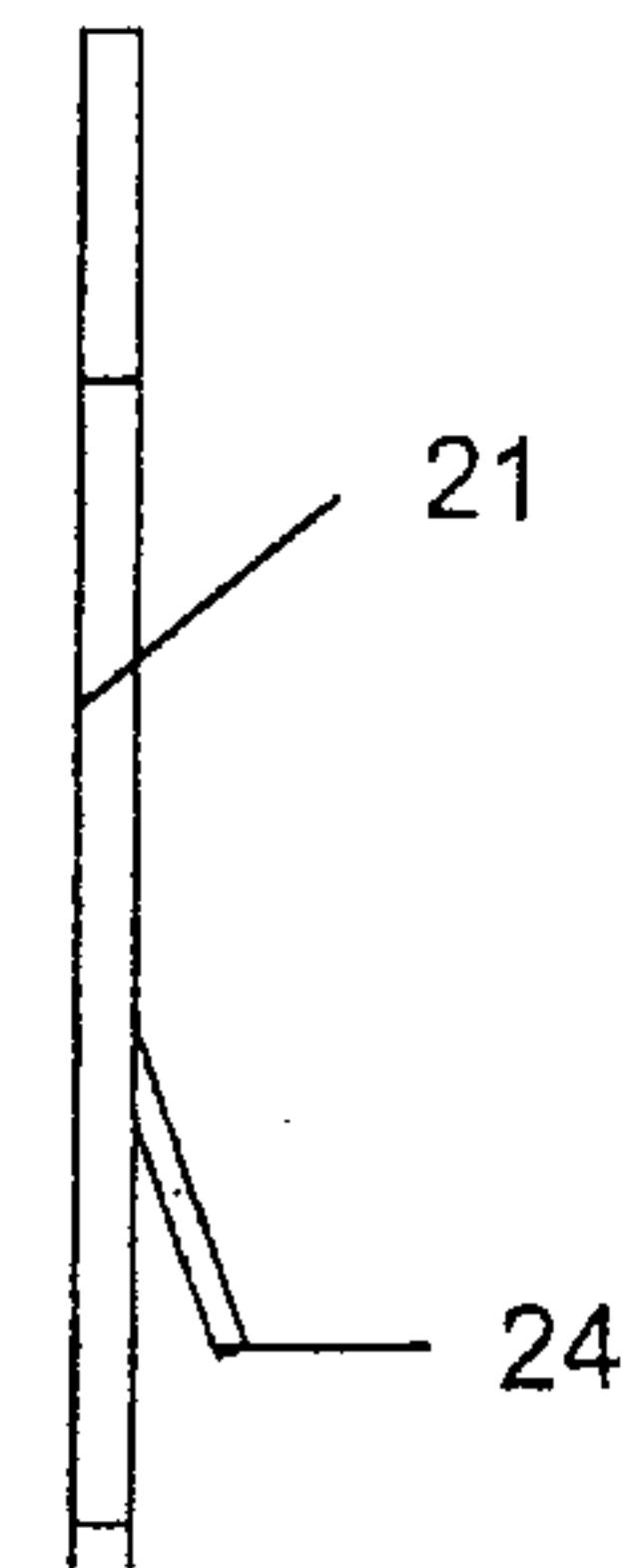


Fig. 11

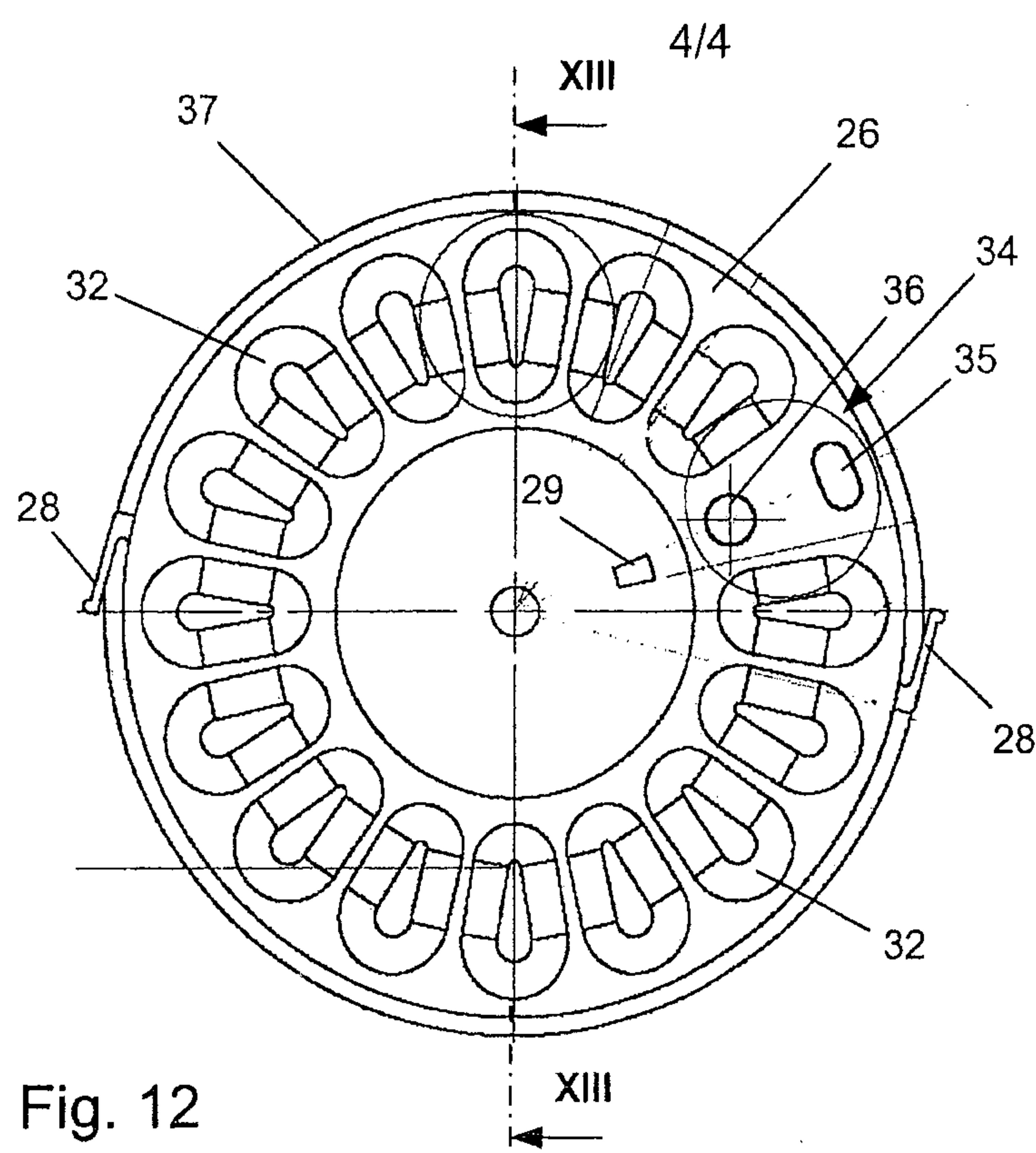


Fig. 12

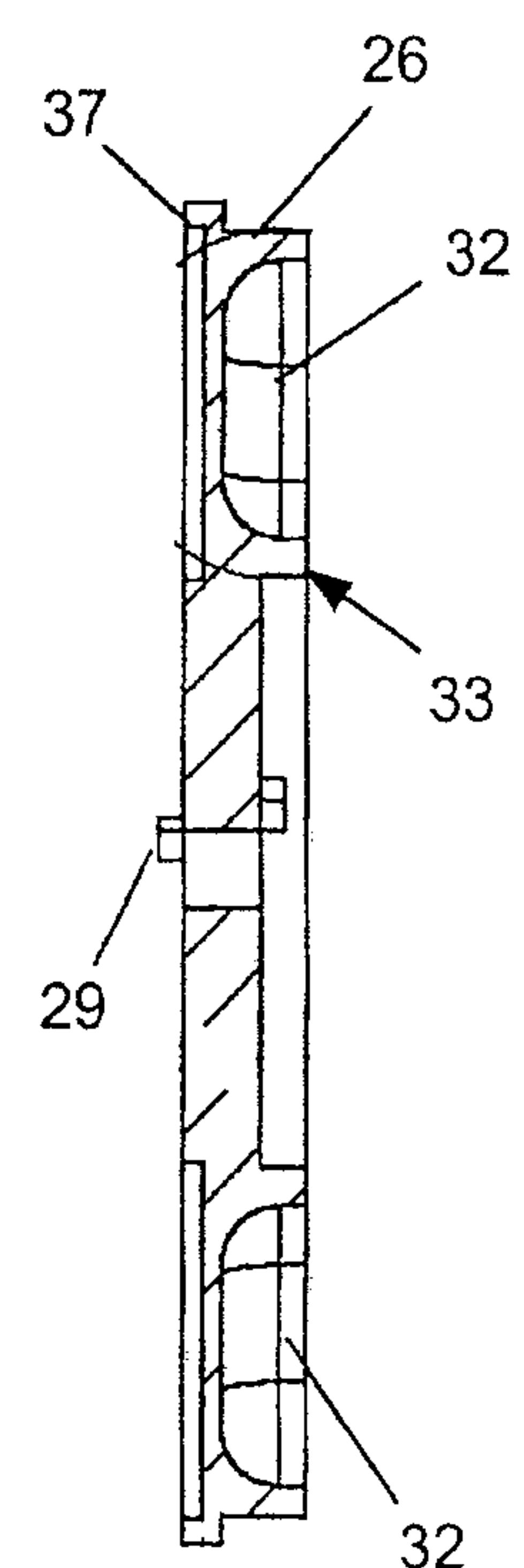


Fig. 13

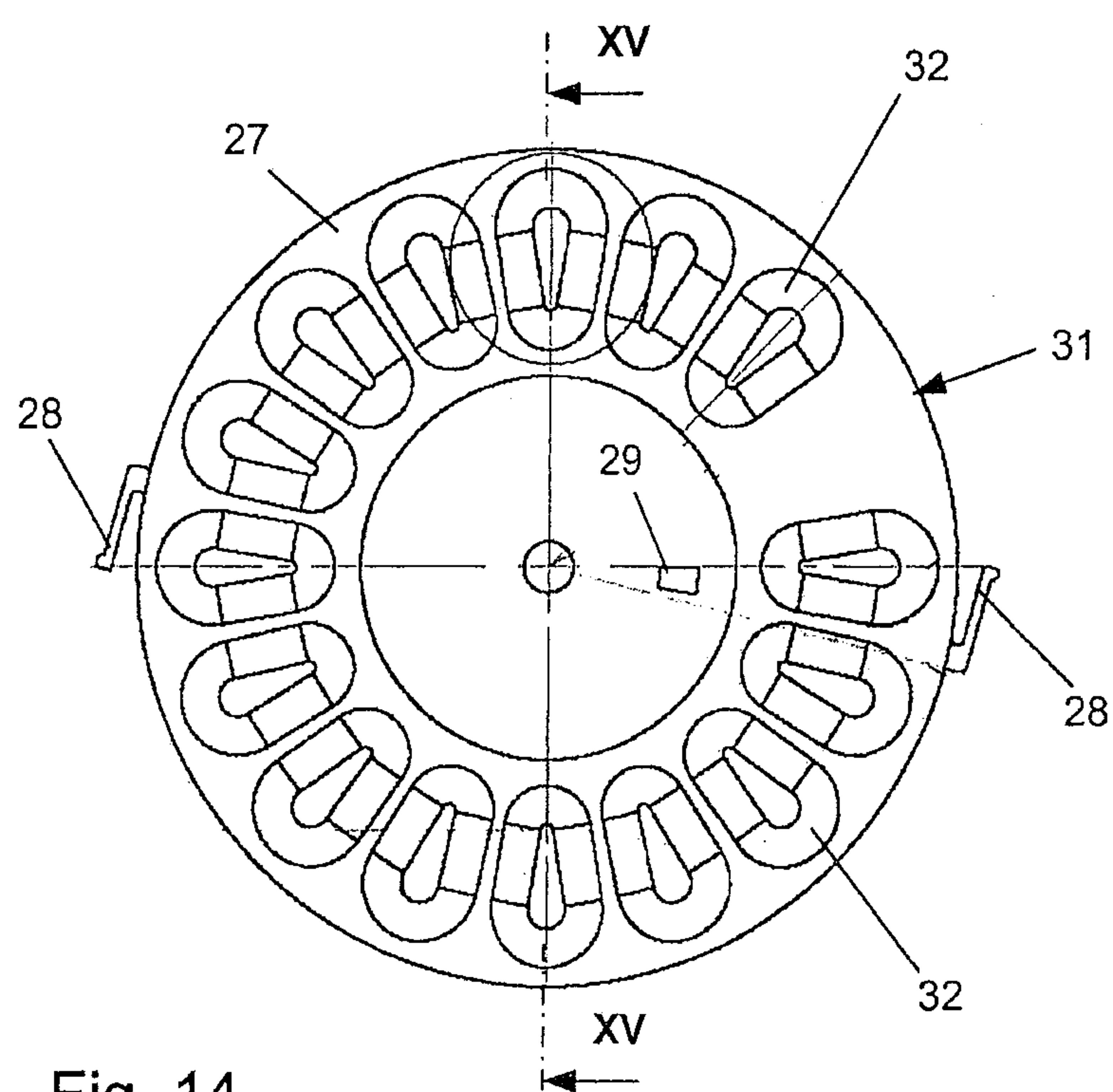


Fig. 14

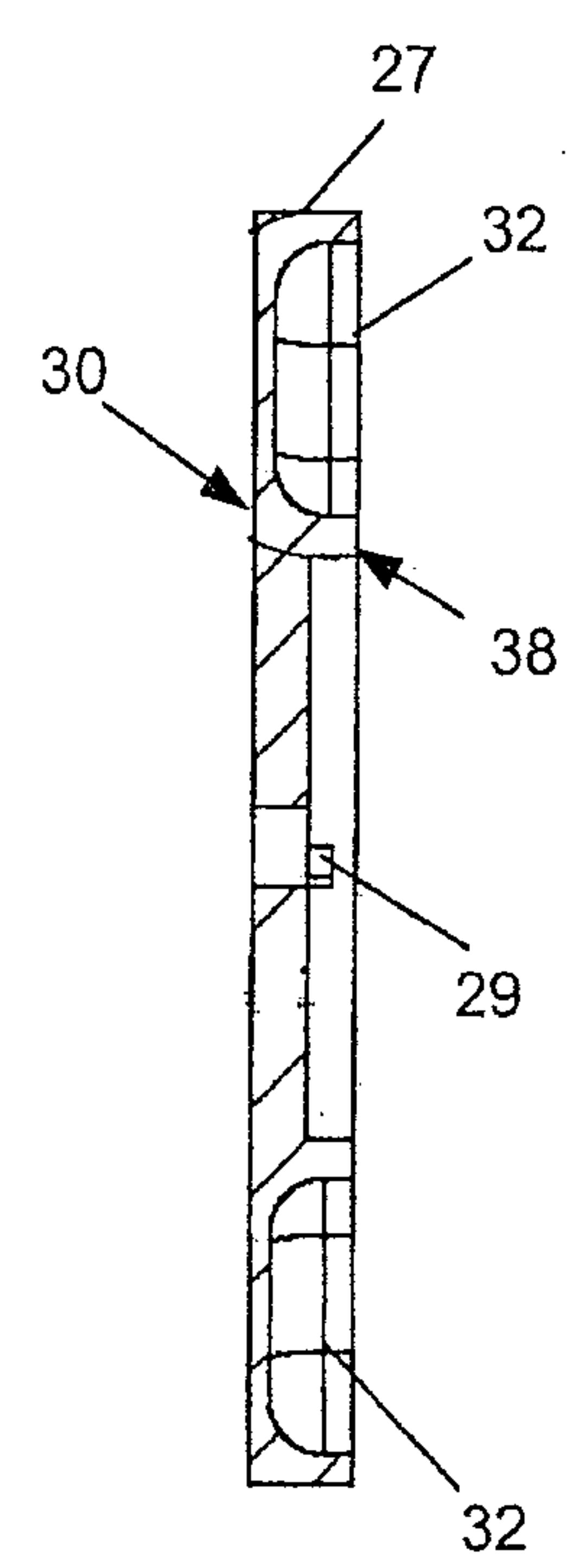


Fig. 15

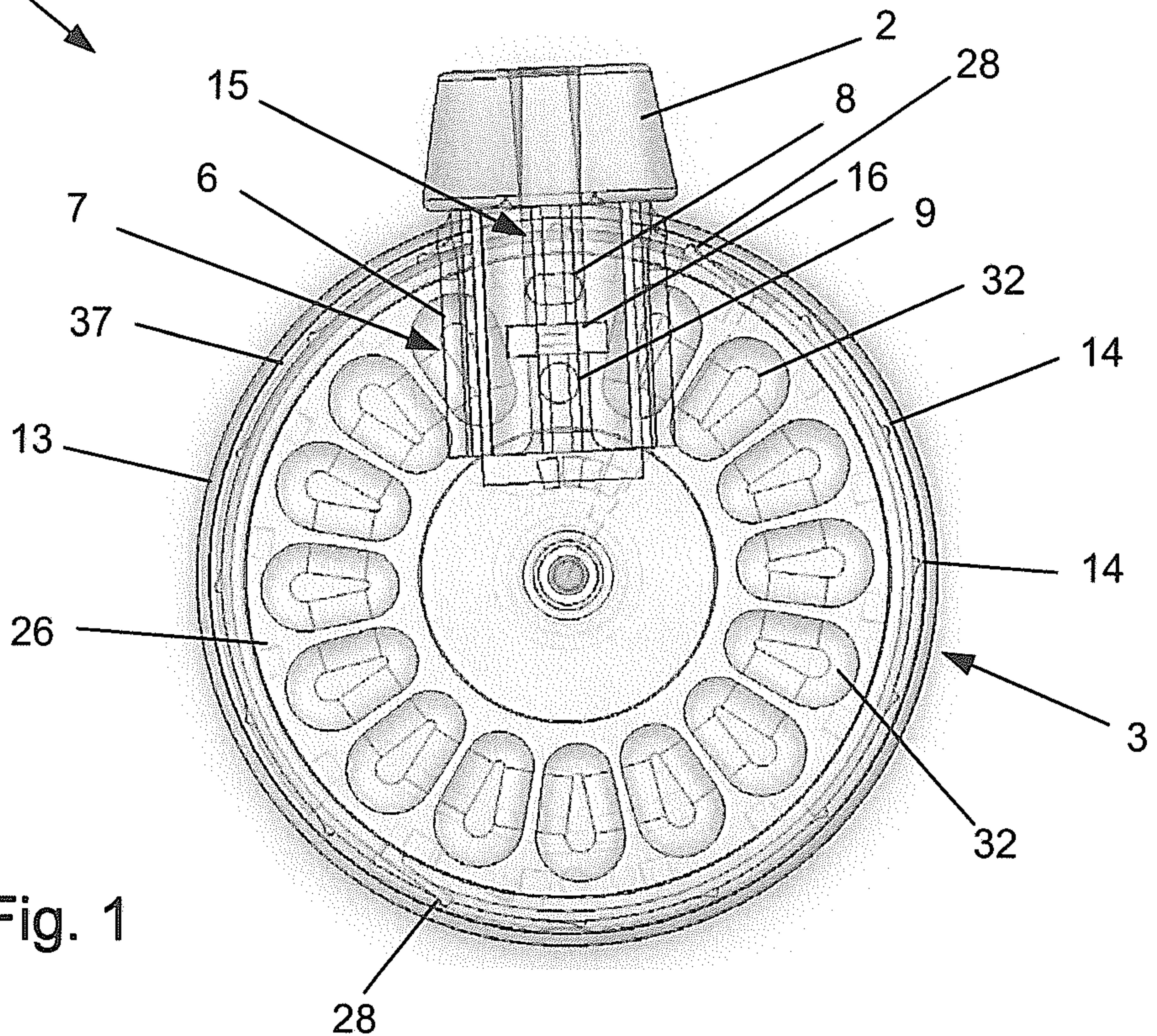


Fig. 1