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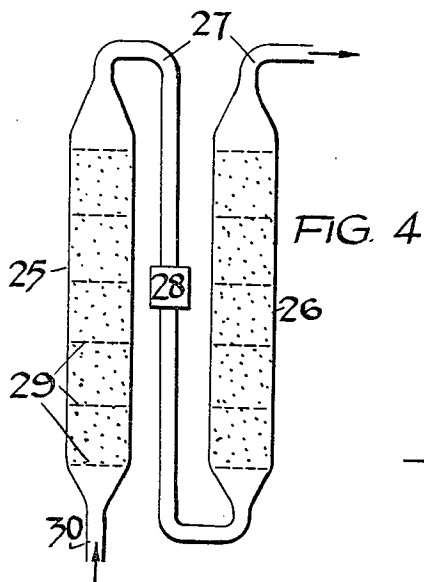
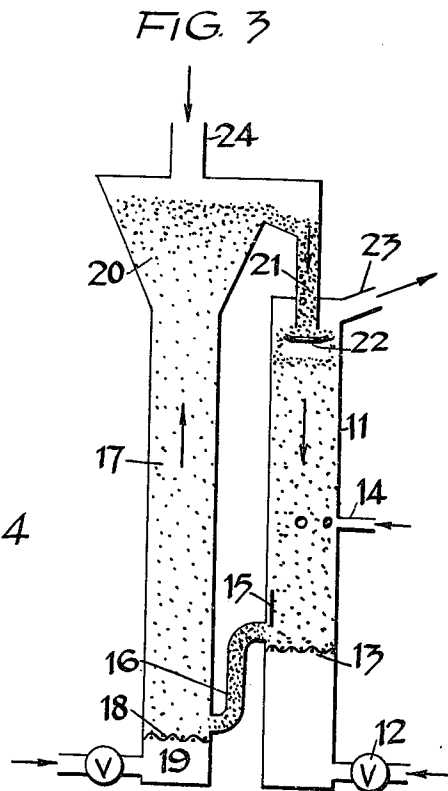
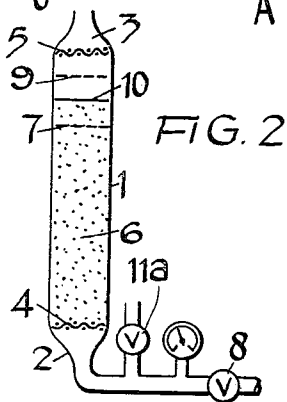
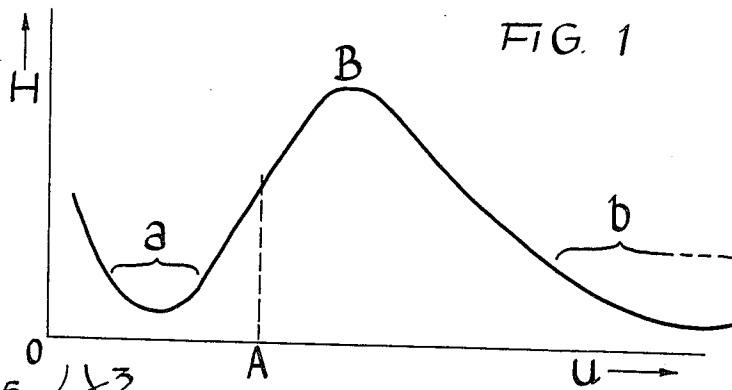
V. PRETORIUS ET AL

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CHROMATOGRAPHY

Filed May 10, 1966

2 Sheets-Sheet 1



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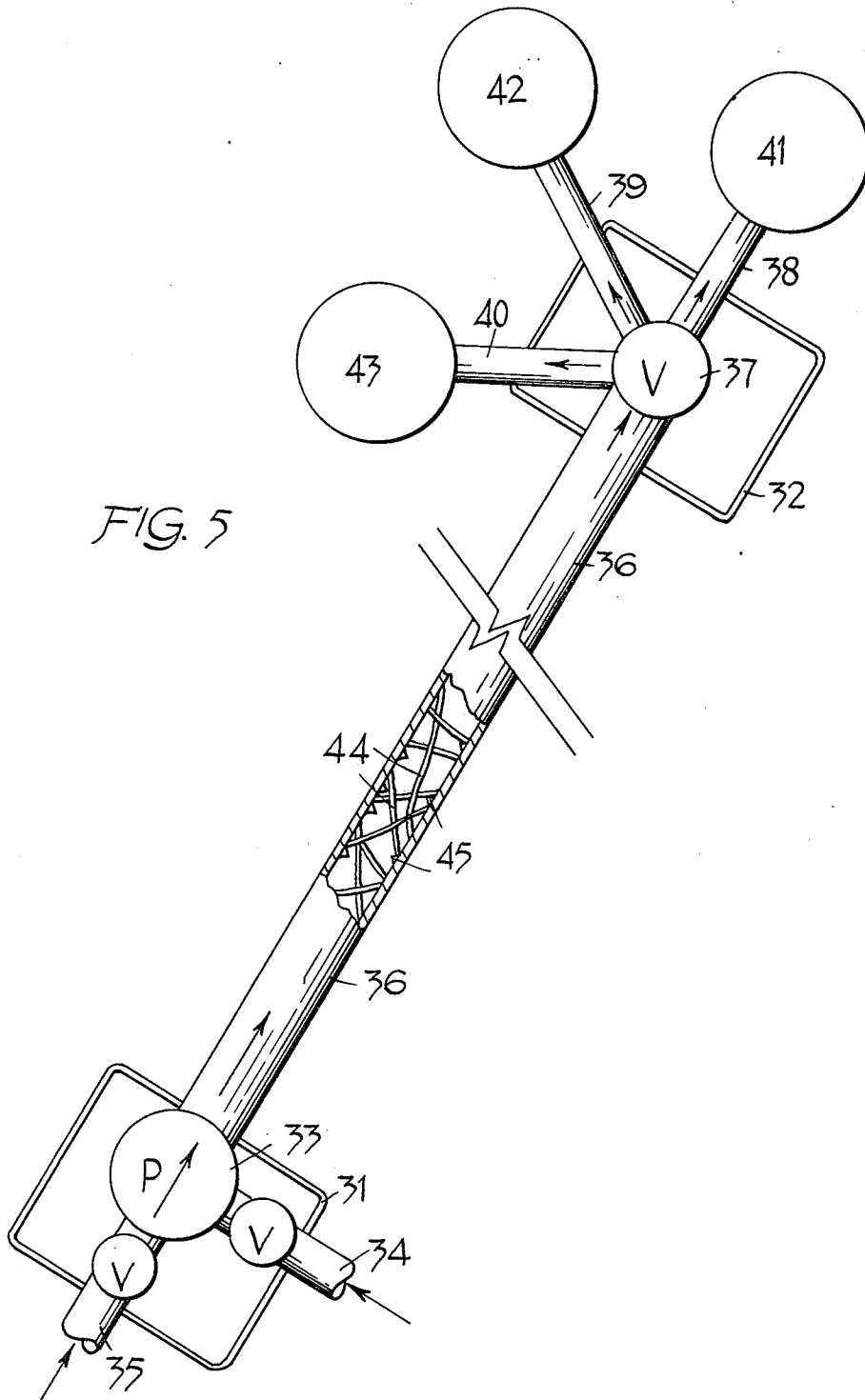
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CHROMATOGRAPHY

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13 Claims

ABSTRACT OF THE DISCLOSURE

In the chromatographic process of the invention, the relative velocity between the forwarding and retarding phases of a chromatographic system is higher than that corresponding to the onset of turbulence in the forwarding phase to decrease the resistance to mass transfer in the forwarding phase. It is also below the value at which the contribution to plate height resulting from the resistance to mass transfer in the retarding phase becomes the overriding factor. In open tube columns the theoretical plate height may thus be lowered to a value about equal to the column diameter; accordingly the invention provides for pipe lines, preferably including turbulence inducing formation to be used for chromatographic separations while substances to be separated are conveyed between two geographically spaced apart localities, such pipe lines for that purpose containing a retarding phase. In the case of packed columns the high velocity of the forwarding phase can also be used to maintain a particulate column packing in an expanded condition offering a lowered resistance to the flow of the forwarding phase. The particulate material may be fully fluidised, porous partitions limiting the movement of the particulate material to a distance not exceeding the theoretical plate height required for the separation, preferably a distance about equal to the column diameter. Alternatively the flow velocity of the forwarding phase is adjusted to a value at which the particulate material is expanded without relative movement between the particles. The free-flowing properties of such expanded bed may be utilised in continuous chromatography wherein the bed is caused to flow uniformly in counter current to the forwarding phase.

The present invention relates to chromatography.

It has been known for some time that for most chromatographic separations there exists a typical relationship between relative speed of movement between the phases on the one hand and that factor of separating efficiency of the column or equivalent which is usually expressed in terms of theoretical plate height on the other hand. As a general rule it is found that this aspect of efficiency improves with speed initially, reaching an optimum at a comparatively low speed manifested by a minimum of theoretical plate height whence the theoretical plate height increases again.

Hitherto it was believed that any speed increase beyond the aforementioned optimum would invariably be accompanied by a correspondingly increased and rapidly becoming unacceptable plate height, and accordingly it was considered advisable to adjust one's separating conditions as closely as possible to the said optimum, compatible with reasonable speeds of operation.

It is one object of the invention to provide a chromatographic separating process which can be adapted to produce very rapid separations in a given system by comparison with the same system employed under conventional conditions and in some cases permitting the short-

ening of separating times by one or more orders of magnitude.

Alternatively it is an object of the invention to allow the attainment of improved separations by permitting the use of a larger number of theoretical plates in a given separating time and/or by the beneficial effect of improved radial mixing of the material forwarding phase in a direction transverse to the direction of net flow.

We have now found surprisingly that, contrary to previous teachings, reduced theoretical plate heights may be experienced once again if the speed is increased beyond a certain limit, subject to certain conditions which may be realised in many chromatographic systems. Under those conditions it is sometimes possible to attain separating efficiencies of a quite acceptable quality, sometimes of the same order as at the first mentioned optimum but at very considerably higher operating speeds. In gas chromatography separation times may be shortened by a factor of 10; in liquid chromatography the time may be shortened by as much as 10⁴ in spite of slightly longer columns in some cases.

Moreover, we have established that these conditions are capable of practical realisation and have explored the factors necessary for the attainment of practical benefits.

A chromatographic separating process in accordance with the present invention comprises: (a) selecting a chromatographic system comprising a tubular passage confining a retarding phase and a material forwarding phase, of which at least the latter flows through said tubular passage, and a material to be separated in phase interchange between said phases, individual parts of the retarding phase being restrained throughout said interchange against movement relative to the overall state of movement of the retarding phase in respect of said passage beyond a limit exceeding the order of magnitude of said passage; (b) selecting said system further for the function of theoretical plate height versus the relative overall speed between the phases to have a first minimum for said plate height in the region of laminar flow of the forwarding phase, thereafter at substantially higher relative speed to have a maximum substantially corresponding to the onset of turbulence in the forwarding phase; and (c) carrying out a chromatographic separation employing said system at a relative speed between the phases in excess of the speed corresponding to said maximum and below a speed at which the contribution to plate height resulting from the resistance to mass transfer in the retarding phase substantially exceeds the contribution to plate height resulting from the resistance to mass transfer in the mobile phase.

We employ the term "relative speed" because the invention is applicable in principle to countercurrent operations, in particular continuous chromatographic separations carried out with both phases moving in opposite directions.

However, the invention is also particularly advantageously and comparatively easily applied to systems in which the retarding phase (e.g. a solid phase or a liquid phase retained by a solid support or a gel) is stationary, whilst the other, the material forwarding phase (e.g. a gas, vapour or liquid phase) is mobile.

The last-mentioned, conventional type of system may be employed using the features of the present invention to achieve chromatographic separations in seconds which previously required minutes or even hours. For analytical purposes this is a great advantage, particularly when applied to process control in industry, since the rapid analytical results can be applied almost instantly to take corrective measures where necessary.

Thus the method can be adapted to process control in the oil and gas manufacturing, refining and processing industry, e.g. in petrochemistry, hydrocarbon synthesis, polymer manufacture and many other organochemical industries. The method is also applicable to various inorganic processes in which the materials being processed are amenable to chromatographic analysis, including the analysis of flue gases in metallurgical processes, e.g. steel refining.

Another aspect of the invention is the vastly increased throughput attainable with a given column or the like, rendering chromatography suitable for separation on a preparative scale where such was previously uneconomical.

In principle the invention is applicable to open tube columns as well as randomly or uniformly packed columns, baffled columns, or any other type of column, but it will be understood that the optimum conditions for gaining the maximum benefit of the invention will differ for each type of column.

Also in accordance with the invention new or improved chromatographic apparatus is provided, suitable for carrying out the above, defined process.

Thus one apparatus in accordance with the invention comprises at least one column subdivided by partitions pervious to the forwarding phase and impervious to the retarding phase and transverse to the direction of flow of the forwarding phase into a plurality of column sections, each having a length not exceeding the order of magnitude of the column diameter and comprising column packing material in said sections which in the fully settled condition of the packing material leaves a space devoid of packing material between one section of packing material and the next.

A further apparatus in accordance with the invention comprises a first upright column, adapted to contain a bed of particulate material comprising the retarding phase in a dense phase, expanded, non-turbulent, freeflowing condition, a bed support pervious to the forwarding phase and impervious to the retarding phase at the bottom of said first column and an inlet for forwarding phase below the bed support, an outlet for forwarding phase containing a separated fraction above said bed support, intermediate between the bed support and said outlet for the forwarding phase an inlet for material to be separated, means for withdrawing retarding phase from a locality below the inlet for the material to be fractionated, and means adapted to receive the retarding phase thus withdrawn, removing therefrom a further separated fraction and returning the retarding phase to the top of the said first column.

The invention may be applied to the separation or concentration of substantially all substances inherently capable of chromatographic separation or concentration and is adaptable to virtually any known type of chromatography e.g. liquid-liquid partition chromatography (including reversed phase), liquid-solid chromatography (where the solid phase may be an adsorbent), ion exchange chromatography, gas liquid chromatography or gas solid chromatography.

The process may be applied to the separation, concentration or purification of pharmaceutically active substances e.g. hormones, vitamins, alkaloids, antibiotics, or essential oils, or of inorganic substances, e.g. the rare earths, purification of uranium, separation of fission products for the recovery of valuable substances therefrom, chromates, recovering of noble metals, e.g. gold, etc.

Pipelines adapted to function as chromatographic apparatus are considered as falling within the scope of the invention.

Having now defined the invention in general terms, the following description, partly with reference to the drawings and by way of example will serve to explain the invention in greater detail.

In the drawings:

FIG. 1 represents a typical example of a graph (not strictly to scale) showing the relationship of relative velocity between phases (U) and theoretical plate height (H);

FIG. 2 represents diagrammatically the employment of a powder-packed column in accordance with one embodiment of the invention;

FIG. 3 represents diagrammatically an apparatus for continuous chromatography in accordance with the invention;

FIG. 4 represents diagrammatically another apparatus in accordance with the invention for carrying out chromatographic separations under fluidised bed conditions; and

FIG. 5 represents diagrammatically in plan view, partly broken away a pipeline for effecting chromatographic separations.

Referring to FIG. 1 of the drawings, portion OA represents a typical curve of H versus U for a randomly packed or open tube column as it had been known to date. It has now been discovered surprisingly that the curve at B passes through a maximum and from there onwards the curve drops, provided the effect is not obscured by too large a contribution to plate height due to the retarding phase, which under all circumstances should be kept as low as feasible. This is achieved by choosing the lowest practical effective film thickness in the retarding phase and where possible choosing the retarding phase such that the concentration distribution coefficient in a given system is high, e.g. of the order of 1000 in the case of gas chromatography and 100 in the case of liquid chromatography. Accordingly, the invention provides for chromatography to be carried out under the conditions represented by that part of the curve which is to the right hand side of B rather than the portion approximately represented by *a*. It will be found that point B coincides substantially with the onset of turbulence in the material forwarding phase.

In typical examples the relative velocity at *a*, i.e. in the vicinity of the first minimum of the curve is of the order of 5 cm./sec. when using a gas as the forwarding phase, and that is the order of velocity generally employed in gas chromatography. The velocity in region *b* corresponding to conditions preferably employed in accordance with the invention differs very considerably, depending on the nature of the column employed (and to some extent on the gas). Using an open, smooth walled pipe of 10 mm. diameter, the velocity will be of the order of 2000 cm./sec. Using a 1 mm. capillary, the velocity becomes of the order of 100,000 cm./sec. In both cases the plate height will approach the value of the pipe diameter under thoroughly turbulent conditions provided the resistance to mass transfer in the retarding phase is sufficiently low.

Using liquid forwarding phases, different values for the velocities will apply, depending particularly on the viscosity of the liquid.

In packed columns the velocity at *a* is generally of the same order as for open tubes, but at *b* the values will vary considerably, depending largely on the nature of the packing.

In the case of open (unpacked) tubes the velocities required for the desired low plate height at *b* can be reduced if desired for any reason by placing judiciously spaced obstructions in the path of the forwarding phase. By judiciously spaced we mean that the spacing does not exceed substantially the distance over which the turbulence inducing effect of the obstruction is effective. For example, struts, e.g., of wire, may be inserted in the tube. The obstructions may also be attached to one or more longitudinal wires, rods or filaments provided inside the pipe, e.g. in the nature of barbed wire strands. The columns may include wire gauze structures of a similar nature as are employed for certain distillation columns.

Grooves or ridges, preferably transverse to the direction of flow may also be provided in the walls to induce turbulence.

All of the above simultaneously help to increase the surface area available to the retarding phase.

Vibrations, in particular ultrasonic vibrations may also be used to induce turbulence at a lower velocity, if for any reason a very high velocity creates problems, e.g. if in a given system the kinetics of exchange constitute a limiting factor, and quite generally to produce advantageous effects.

Portion *b* of the curve will not drop indefinitely but will rise eventually when the contribution to plate height resulting from the resistance to mass transfer in the retarding phase begins to exceed the contribution to plate height resulting from the forwarding phase. Because any increase in flow rate involves (sometimes substantial) increases in pressure, it will normally be uneconomical to increase the flow rate much beyond that point.

It is possible to determine the individual contributions to plate height separately. The contribution resulting from the forwarding phase alone (including flow profile effects) may be measured in a known manner when retention is excluded. The total theoretical plate height may also be determined in known manner, and the difference between the two is equivalent to the contribution of the retarding phase.

In order to keep the contribution of the retarding phase as low as possible it is advantageous to employ a retarding phase in which material exchange is confined to the immediate vicinity of the surface. This condition is fulfilled for example by many solid adsorbents (particularly non-porous adsorbents like metals, glass, or porous substances substantially devoid of blind pores, e.g. some types of activated charcoal, alumina, silica gel, molecular sieves and even organic polymers, e.g. cross-linked polymers of styrene, divinyl benzene or their derivatives or interpolymers); thin liquid films and thin layers of ion exchangers. Such thin films should preferably not exceed 10^{-3} cm. and be preferably not in excess of 10^{-4} cm. In the case of ion exchangers monomolecular layers of ion exchanger are feasible and preferred. For example, synthetic ion exchanger films on a support may be employed (e.g. produced by polymerisation of divinyl benzene styrene to form a thin film on a support, followed by sulphonation). It is also possible to subject the surface of plastic capillaries or powders, e.g. polyethylene or polyvinyl chloride to sulphonation.

The aforesaid applies equally to open tube and packed columns.

Not only in the case of open tube columns but also in packed columns it is desirable for the turbulence of the forwarding phase to extend over the entire column width. This not only serves to assure thorough contact of all parts of the forwarding phase in a minimum of time with the retarding phase but also flattens the flow profile of the forwarding phase due to the advantageous effect of thorough radial mixing. Advantageously complete radial mixing should take place repeatedly and within distances not exceeding the order of magnitude of the column or passage diameter. This can be achieved, for example, solely by means of the effect of thorough turbulence, although it may be aided by vibrations as mentioned further above or various mechanical means, some of which will be referred to below in different contexts.

Because of the high speeds inherent in the process it becomes practical to carry out chromatographic separations in pipelines which, in accordance with the invention are specially adapted as chromatographic separating apparatus, thus combining chromatographic separations, e.g. purifications of materials, with the step of conveying such materials from one locality to another distant locality. It has been observed that when employing the conditions herein specified in an unpacked tube, the walls of which comprise a surface serving as a stationary phase, the theo-

retical plate height equals by approximation the diameter of the tube. It will thus be readily understood that a pipeline a foot or more in diameter and several miles long corresponds to a considerable number of theoretical plates and allows difficult separations to be achieved on large volumes of material in a reasonable time. Elution development types of separation may, for example, be carried out semicontinuously by introducing the solute material to be separated pulsewise in the form of slugs; in this manner an efficiency corresponding to about 85% of fully continuous operation may be attained in a quite uncomplicated manner.

The comparatively low chromatographic capacities of pipe-lines in which only the pipe wall inner surface is available for material exchange sites of the stationary phase is no great disadvantage in those cases where a valuable substance present in low concentration is to be enriched or isolated or where a minor contaminant is to be removed from a material to be purified. Such separation problems are quite frequent. Pipe walls may, however, be treated or coated in manners known per se to increase the specific surface area.

Enrichment or isolation of a valuable minor component is possible by frontal analysis, a technique which is particularly interesting commercially when applied to pipe-lines in those cases where the medium employed to purge the pipe-line between successive separations is itself also a substance which it is desired to transport from the one end of the pipe-line to the other. These types of separation may be applied to the separation of the components of materials which are traditionally conveyed by pipe-line, including gases, vapours, and liquids, e.g. natural or synthetic petroleum products, organic solvents, coal distillates and pyrolysates, inert gas concentrates, e.g. helium enriched from natural gas, fractions derived from the distillation of air.

The invention may also be applied to the separation of isotopes. Hydrogen gas when conveyed as described through suitably prepared pipe-lines will arrive at the other end wholly or partly separated into isotopes. Similarly heavy water may be produced from steam. Deuterium concentrates may also be obtained by conveying hydrocarbon gases through pipe-lines in the manner described.

When desired or required all the said separations and many others may also be carried out on a large or small scale in apparatus performing no dual function such as conveying the material from one locality to another.

There is no need in the context of the various possible applications referred to above to give a detailed description of each, since the forwarding and retarding phases employed and other conditions may be essentially the same as are employed in conventional chromatography for the same separations at slow relative speeds between the phases. The difference resides in the very much higher flow rates employed to attain typical turbulent flow conditions and the greater than usual care in the selection and/or preparation of the retarding phase to keep the plate height contribution of the latter to a minimum.

The flow velocity required to achieve proper turbulence in the moving phase as a prerequisite for a low theoretical plate height may in some cases be very high in an open tube such as a pipe-line. If operation at lower flow velocity is desirable, e.g. in order to economise on pumping equipment and energy, it is feasible to install judiciously spaced apart or continuous turbulence inducing bodies inside the pipe-line as will be readily understood and which will assist in achieving radial mixing of the forwarding phase. The surface texture of the pipe wall may also be modified to assist in the production of turbulent conditions. Such measures may simultaneously serve to increase the surface area available for active exchange sites.

In some cases the pipe material itself, e.g. metal may be employed as a stationary phase, if necessary after

suitable activation. An aluminium pipe surface may be subjected to oxidation in a manner known per se to produce an active alumina surface. Pipes may also be coated internally by precipitation of a film of colloidal carbon, ion exchange resin, silica gel or other active substance, including a liquid film.

To improve separations and separating capacity whole pipe-lines adapted for the process may also be packed with a stationary phase or a support carrying a stationary phase.

Packed columns, regardless of size, which may be employed in the process, require no special description, since they may be essentially identical with conventional columns, except that the wall strength may have to be dimensioned to withstand higher pressures necessary for the attainment of high flow rates.

In this context it has been found that for the greatest overall benefits to be attained, the particle size in various forms of packed columns should at least be 0.5 mm. in diameter and preferably at least 1 mm.

FIGS. 2, 3 and 4 illustrate a modification of the process allowing the attainment of high flow rates with considerably less pressure. This is achieved by employing the retarding phase in a column bed of particulate material, maintained by the flow of the turbulent forwarding phase at a bulk volume larger than the bulk volume of the particulate material in its loosest condition.

Referring now to FIG. 2 the column 1 comprises a fluid inlet 2 and an outlet 3 separated from the column interior by screens 4 and 5 respectively pervious to the forwarding phase but impervious to the particulate packing 6 in the form of a loose bed. In its loosely settled condition the packing fills the column to level 7. Prior to the actual separation the fluid constituting the forwarding phase is introduced at 2 at a rate controlled by valve 8 sufficiently high for the particulate material to become fully fluidised without becoming entrained in the forwarding phase. The packing in its fluidised condition (i.e. a condition in which the packing particles are in thoroughly turbulent movement) reaches a level 9. The flow rate of the forwarding phase is now reduced sufficiently for turbulence of the packing particles to cease, which is accompanied by a certain shrinkage of the bed, say to level 10. In this condition the bed has the following important characteristics: It has a lower bulk density and higher porosity than the bed in its loosest condition to which it would settle in the absence of any flow of forwarding phase. Accordingly, for a given pressure drop through the column the flow velocity of the forwarding phase will be higher than the flow velocity resulting from the same pressure drop through the bed prior to the step of full fluidisation. The bed also has free flowing properties almost equal to those of the bed in the fully fluidised condition. However, the uncontrolled turbulence of the particles which would result in band widening is absent, whilst conditions are so chosen that the forwarding phase is well inside the turbulent range and capable of flowing freely in all dimensions of the loosened up bed. The material to be separated is introduced at 11a. The fractions are collected one by one from the effluent at 3.

In principle the forwarding phase in this embodiment may be a liquid in which case the retarding phase packing may be solid throughout or particles of a solid support coated with a film of liquid retarding phase or gel or beads of a gelatinous retarding phase, e.g. a resinous or rubbery polymer, say, for example, having ion exchange properties.

In the case of a liquid forwarding phase partition 4 is preferably in the form of a wire screen offering a minimum of flow resistance. A reasonable pressure drop through the bed support 4 is an advantage when employing a gas as the forwarding phase which is preferred with this type of apparatus. For example, a closely woven synthetic fibre filter cloth supported on any rigid perforated or gridlike support will give good results. Porous

ceramic plates or sinter glass plates may also be employed. Metal plates with fine perforations may sometimes be employed successfully. Felt is usually less satisfactory. The best support for any particular column packing may be determined by simple experiment.

The packing material should preferably be composed of rounded, e.g. approximately spherical, particles, which should preferably be substantially free of random projections or radial structures liable to result in interlocking of the individual particles. A tendency towards lump formation is a disadvantage and should be avoided. Suitable particle sizes will depend, inter alia, on the nature, e.g. shape and specific gravity, of the powder particles, but will usually be in the range 10-500 mesh, ASTM, the larger sizes applying to powders of low specific gravity. The particles may for example be composed of silica gel, alumina, magnesium silicate, various metals, glass, activated carbon, various organic or inorganic solid adsorbents, natural or synthetic polymers, solid or gelatinous ion exchangers or other substances as will be understood by those skilled in the art.

Data are available allowing calculation or estimation of the most favourable particle size for a given system. Assuming for example that a gas having the density and viscosity of air at normal temperature and pressure is to be employed as the forwarding phase, assuming further that the retarding phase has the density of silica gel or glass beads and is composed of near spherical particles of substantially uniform size, the minimum favourable particle size is in the vicinity of 0.5 mm., since at that particle size a linear gas velocity of the order of 1 m./sec. may be attained without fluidising the powder. Such speed is already clearly in the turbulent range. More advantageous will be a powder at least of the order of 1 mm. in diameter.

Under turbulent flow conditions the pressure drop in an expanded non-fluidised bed as described above can be as much as twenty times less for a given flow rate than when the bed is firmly packed.

The condition just described is also characterised by a high degree of free flowing ability which renders the condition particularly suitable for continuously feeding a bed of retarding phase through a tube in countercurrent with the forwarding phase in a continuous chromatographic process.

Referring now to FIG. 3, the bed condition described with reference to FIG. 2 is applied to a continuous chromatographic process. The actual separating column is indicated by 11 and contains a packing maintained in the condition just described by a flow of forwarding phase entering through inlet 12 and bed support 13. Material to be separated is introduced continuously at 14. At the bottom end of the column the free flowing packing material is continuously withdrawn under gravity at a rate adjusted by gate 15 and flows in a condition denser than in column 11 through standpipe 16 into the stripping column having a bottom screen 18 separating the column from space 19 from which a stripping medium is introduced into the column to produce a highly turbulent, preferably fluid entrained condition in column 17. Since the material in column 17 has a much lower bulk density than the material inside column 11, a circulatory flow of packing material results through column 17 towards the broadened top 20 where, due to decreasing flow velocity of stripping medium, settlement of packing material takes place. The material settling out at 20 returns under gravity via standpipe 21 and baffle 22 to the top of column 11. The rate of circulation of the retarding phase is so adjusted in relation to the feed rate of the forwarding phase that one desired fraction of the material leaves column 11 together with the forwarding phase at outlet 23, whilst another fraction leaves column 11 with the retarding phase at 15. This second fraction is stripped off the retarding phase in stripping column 17

and leaves the apparatus with the stripping medium through outlet 24.

Dust separators, e.g. cyclones may be provided if required at outlets 23 and 24. Portion 20 of column 17 may also incorporate the features of a cyclone or equivalent device.

It will be readily understood that the circulation of retarding phase may also be assisted, if desired or required, by mechanical means. It is not essential that gravitational effects be relied upon exclusively or at all, although, where practical, such will contribute to the simplicity of the apparatus.

The stripping medium may be the same as the forwarding phase, in which case the spaces underneath bed supports 13 and 18 may be in communication or even integral with one another. In the latter case it is advantageous for the bed support 18 to offer less resistance to flow than bed support 13 in order to produce a condition of lower bulk density in column 17 than that prevailing in column 11.

Any other medium suitable for preparing the retarding phase for re-use in column 11 may be employed. For some purposes it is even possible to employ the starting material which is to be separated as a stripping medium and recycling the effluent from outlet 24 wholly or partly to inlet 14. This embodiment is particularly useful for purifying a substance in which the contaminant is a minor component. It is furthermore possible to carry out the stripping of retained material off the retarding phase in stages and fractionally by substituting a plurality of columns in series for column 17.

The apparatus is particularly suitable for gas chromatography but may in principle also be designed for use with a liquid forwarding phase.

Referring now to FIG. 4, columns 25 and 26 of which any number may be connected in series as shown by means of connecting pipes 27 which, if desired, may incorporate booster pumps 28. Each column is subdivided into compartments by screens 29 of a type offering little flow resistance to the forwarding phase (introduced at 30) but forming a barrier to the retarding phase. The heights of the individual compartments between successive screens 29 should be of the same order of magnitude and preferably at the most as large as the optimum plate height attainable with the apparatus, i.e. the same order as the column diameter. Each compartment contains particulate retarding phase material, but insufficient to fill the entire compartment when the material is loosely settled. The apparatus is operated under such conditions of flow velocity of the forwarding phase that the particulate material enclosed in the compartments is maintained in a fully fluidised, i.e. turbulent condition. It is possible in principle to operate this apparatus under dense phase or dilute phase fluidised conditions. Complete radial mixing not only of the forwarding phase but also of the retarding phase is thus assured. Further complete mixing takes place in each booster pump.

Referring now to FIG. 5 the two terminal stages of a pipeline are diagrammatically represented by 31 and 32 respectively, being at geographically spaced apart localities, e.g. at entirely different localities of a large chemical plant or even many miles apart. Station 31 comprises a booster pump 33, into which, as in conventional pipelines lead a plurality of valve controlled feed pipes 34 and 35 for the admission of liquid or gas to be conveyed one after the other from various sources to the terminal station 32 through the pipeline proper 36.

As in conventional pipelines the terminal station 32 is provided with valve means diagrammatically indicated by 37 to divert different products as they arrive one after the other through different branch lines 38, 39 and 40 and to separate containers 41, 42 and 43.

In accordance with the present invention the inside of the pipes of pipeline 36 is coated with a very thin layer of the desired substance which is to serve as the stationary

retarding phase. The pump 33 must be so dimensioned that the velocity of the fluid pumped through the pipeline 36 is within the range of turbulent flow. However, in order to lower the velocity at which such turbulence takes place, the pipeline includes random obstructions 44 in the wake of which turbulence will be induced. In addition, or as an alternative the pipe walls may comprise inwardly directed projections 45 which are similarly designed to induce turbulent conditions. The turbulence inducing formations 44 and 45 also carry on their surface a retarding phase.

In principle the embodiment in accordance with FIG. 5 may be operated substantially in a manner of any one of a variety of known chromatographic separating processes, apart from the feature of high velocity in the range of turbulent flow which is prerequisite for the use of a pipeline to achieve chromatographic separations in practice. Elution chromatography lends itself particularly well to the method. In that case alternate plugs of one substance to be fractionated and another fluid (preferably itself of a type which it is desired to convey to terminal station 32) suitable as an eluent for the fluids being separated, are injected through feed pipes 34 and 35 respectively. As a plug of fluid to be fractionated progresses from 33 to 37, at the same time being partly overtaken by the immediately following unretarded plug of eluent, the least strongly retarded component will become concentrated as a band in the front portion of the pair of plugs. On arrival of the plug at valve 37, the valve will be operated to admit the first band (containing also eluent) through outlet pipe 38 into tank 41. As soon as the end of the first band is approached the valve 37 may now be operated to pass an intermediate fraction of the plug through outlet 39 into tank 42, and when a further desired band arrives at 37, the stream of fluid is diverted through outlet 40 into tank 43, until the first fraction of the next plug to be fractionated arrives when the cycle will be repeated.

It is of course possible to include in outlet pipes 38, 39, 40 conventional means e.g. adsorbents or refrigeration units for the separation of the fractions from the eluent. It has been established by one of the applicants (S. M. Gordon and Victor Pretorius, *Journal of Gas Chromatography* 2, 196 (1964)) that by the injection of alternating plugs into a chromatographic column, it becomes possible to utilise the separating capacity of a chromatographic system with an efficiency of about 80% of the theoretical value corresponding to fully continuous operation, which is very good indeed when bearing in mind the simplicity of the method in which the separation is virtually a by-product of the conveyance of the material between two places.

The arrival of the various substances at valve 37 can be detected by conventional detecting means in a manner known per se.

From the above it will be seen that the problems of recovering the more strongly retarded component of a mixture even from miles of pipeline are no different than in the case of a short conventional laboratory column and that conventional pipelines and ancillary equipment require little or no modification apart from the inclusion of a retarding phase and preferably of obstructions 44, 45 to render such pipelines suitable for the new process.

The following few examples are picked at random to show but a few of the vast number of potential applications of the invention.

EXAMPLE 1

Separation of palmitic acid and stearic acid

The acids are separated by reversed phase partition chromatography. System:—medicinal paraffin as retarding phase, 70% aqueous acetone as forwarding phase, temperature 35° C. The alpha value in this example is 1.7.

(a) Conventional packed column, laminar flow.—Kieselgur serves as the support. A column height of 85

11

cm., a diameter of 8 mm. and a pressure head of 50 cm. solvent is employed. Analysis time: appr. 3 hours.

(b) Packed column, turbulent flow.—Glass beads, 1 mm. diameter, treated with dichlorodimethyl silane to serve as the support. The support is impregnated with a dilute solution of the medicinal paraffin in ether. After evaporation of the ether the film thickness is appr. 10^{-4} cm. The column length is 2.5 m. and pressure drop 5 atm. resulting in a separation time of approximately 50 seconds.

(c) Open tube, laminar flow.—A very small bore tube, diameter 0.2 mm. is chosen (a larger diameter of say 2 mm. would lengthen the required column length about tenfold and the analysis time a hundredfold). The column length is 100 cm., the pressure head 30 cm. of solvent and the separation time 2 hours.

(d) Open tube, turbulent flow.—Here a large, say 2 mm. diameter tube is preferred because, although a 0.2 mm. capillary would theoretically make separation times of less than 1 sec. possible, the pressure drop necessary therefore would be of the order of 3000 atm. which is too high in practice. The column length is 40 m., the pressure drop 35 atm. and the separation time 4 minutes.

EXAMPLE 2

Separation of transbutene-2- and butene-1 by gas/liquid chromatography

This example is illustrative of separation problems arising in the field of petrochemistry.

The following system is used: retarding phase: diisodecyl phthalates; forwarding phase: N_2 50° C. Alpha for this system is approximately 1.3.

(a) Open tube, laminar flow:

Tube diameter -----mm-- 0.2
Separation time -----sec-- Appr. 10
Column length -----m-- 10
Pressure drop -----atm-- Appr. 10

or:

Tube diameter -----mm-- 2
Separation time -----min-- Appr. 4
Column length -----m-- 50
Pressure head -----cm. solvent-- 30

(b) Open tube, turbulent flow:

Tube diameter -----mm-- 0.2
Separation time -----sec-- <1
Column length -----m-- 10
Pressure drop -----atm-- Appr. 200

or:

Tube diameter -----mm-- 2
Separation time -----sec-- Appr. 10
Column length -----m-- 200
Pressure drop -----atm-- Appr. 90

(c) Apparatus in accordance with FIG. 4:

Particle size -----mm-- 0.5
Total column length -----m-- 25
Diameter -----cm 10
250 sieves spaced 10 cm. apart.
Flow rate -----m./sec-- 5
Separation time -----min-- Appr. ½

(d) Apparatus in accordance with FIG. 2:

Particle size -----mm-- 1
Column length -----m-- 10
Column diameter -----cm-- 20
Flow rate -----m./sec-- 1
Separation time -----min-- appr. 1

¹ 5 sections of 2 m. in series.

Note.—In (c) and (d) the exact flow rate is determined empirically for each packing material because of its critical variation with minor differences in particle shape and size.

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(e) Apparatus in accordance with FIG. 3:

Particle size -----mm-- 1
Length of column 11 -----m-- 10

Inlet 14 is halfway up, downwards movement of packing: 20 cm./sec.; upward flow of gas: 70 cm./sec. (relative to column walls); column vibrated; flow rate in column 17: appr. 20 m./sec.; diameter of column 17 is ½ of that of column 11 in this example and blow nozzles may be provided at 18 in the manner known from pneumatic conveying equipment.

EXAMPLE 3

Separation of codeine from heroine

This example is typical of alkaloid separations. The following system is used: retarding phase: silicon gel; forwarding phase: methanol-n-butanol-benzene-water, 60:15:10:15. Alpha for this system is approximately 1.4.

(a) Packed column, laminar flow (fine particles):

Separation time -----hrs-- Appr. 25
Column length -----m-- 2
Pressure head -----cm. solvent-- 30

(b) Packed column, turbulent flow (packing material 1 mm. particle size):

Separation time -----min-- 2½
Column length -----m-- 4
Pressure drop -----atm-- 15

(c) Open tube, laminar flow:

Separation time -----hrs-- 8
Column length -----m-- 4
Pressure head -----cm. solvent-- 40
Column diameter -----mm-- 0.2

(d) Open tube, turbulent flow:

Separation time -----min-- 8
Column length -----m-- 50
Pressure drop -----atm-- 40
Column diameter -----mm-- 2

EXAMPLE 4

Separation of atropine from morphine

Retarding phase: silica gel; forwarding phase: benzene-acetone-ether-10% aq. ammonia, 4:6:1:0.3. Alpha for this system is approximately 1.45.

(a) Packed column, laminar flow (fine packing, conventional):

Separation time -----hrs-- Appr. 15
Column length -----m-- 1.5
Pressure head -----cm. solvent-- 30

(b) Packed column, turbulent flow (packing material 1 mm. particle size):

Separation time -----min-- 2
Column length -----m-- 3
Pressure drop -----atm-- 10

(c) Open tube, laminar flow:

Column diameter -----mm-- 0.2
Column length -----m-- 4
Pressure head -----cm. solvent-- 40
Separation time -----hrs-- 9

(d) Open tube, turbulent flow:

Column diameter -----mm-- 2
Column length -----m-- 40
Pressure drop -----atm-- 35
Separation time -----min-- appr. 5

(e) Apparatus in accordance with FIG. 4:

The separation requires (for 99% purity) approximately 100 plates. Choosing a column diameter of 10 cm., the column will be 10 m. long, containing 100 sieve plates and silica gel beads to fill each compartment half full. The bead diameter is chosen so

that the material is fully fluidised at a flow rate of 2 m./sec. The separation will be completed in approx. 1 minute.

EXAMPLE 5

Separation of sodium from potassium

Retarding phase: Ion exchange resin "Amberlite I.R. 100"; forwarding phase: 0.1 N HCl. Alpha in this system is approximately 2.3.

(a) Packed column, laminar flow.—Conventional fine column bed 40 cm. long, 1 cm. diameter. Pressure head: 30 cm. of eluant. Separation time: 11 hours.

(b) Packed column, turbulent flow.—1 mm. particles packed to a height of 1.5 m. Pressure drop: 3 atm. Separation time: appr. 30 secs.

What we claim is:

1. A chromatographic separating process which comprises:

(a) selecting a chromatographic system comprising a tubular passage confining a retarding phase and a material forwarding phase of which at least the latter flows through said tubular passage, and a material to be separated in phase interchange between said phases, individual parts of the retarding phase being restrained throughout said interchange against movement relative to the overall state of movement of the retarding phase in respect of said passage beyond a limit exceeding the order of magnitude of said passage;

(b) selecting said system further for the function of theoretical plate height versus the relative overall speeds between the phases to have a first minimum for said plate height in the region of laminar flow of the forwarding phase, thereafter, at substantially higher relative speed to have a maximum substantially corresponding to the onset of turbulence in the forwarding phase; and

(c) carrying out a chromatographic separation employing said system at a relative speed between the phases in excess of the speed corresponding to said maximum and below a speed at which the contribution to plate height resulting from the resistance to mass transfer in the retarding phase substantially exceeds the contribution to plate height resulting from the resistance to mass transfer in the mobile phase.

2. A process as claimed in claim 1 in which the retarding phase is employed in a column bed of particulate material, maintained by the flow of the turbulent forwarding phase at a bulk volume larger than the bulk volume of the particulate material in its loosest settled condition.

3. A process as claimed in claim 2 which comprises adjusting the flow rate of the forwarding phase relative to the retarding phase to a value at which the particles comprising the retarding phase are in a turbulent, fluidised condition and mechanically confining the turbulent movement of the particles in the longitudinal direction within limits not exceeding the order of magnitude of the transverse passage diameter.

4. A process as claimed in claim 2 in which the flow rate of the forwarding phase is controlled to maintain the retarding phase in an expanded non-turbulent condition whilst turbulent conditions prevail in the forwarding phase.

5. A process as claimed in claim 4 applied to a continuous separation, which comprises:

(i) directing upwards the forwarding phase through said passage at a rate designed to maintain all of said retarding phase within the flow path of the forwarding phase in said expanded, non-turbulent condition;

(ii) introducing continuously material to be separated into contact with the forwarding and retarding phases at a locality of introduction intermediate between the upper and lower ends of the retarding phase within said flow path at a constant predetermined rate adapted to the separating capacity of the system;

(iii) withdrawing the forwarding phase together with a fraction separated out of the material to be separated at said upper end;

(iv) causing the retarding phase to flow under gravity substantially uniformly towards said lower end by withdrawing at said lower end retarding phase continuously at a rate designed to cause the aforesaid fraction to advance in the direction of flow of the forwarding phase and to cause a second fraction to be withdrawn together with the retarding phase at said lower end;

(v) conducting the retarding phase thus withdrawn into the bottom end of a second passage;

(vi) introducing a fluid medium capable of eluting the second fraction from the retarding phase into the bottom end of said second passage at a rate designed to lift the retarding phase to the upper end of said second passage;

(vii) separating and withdrawing at the upper end of said second passage the said fluid medium containing at least a substantial part of said second fraction; and

(viii) returning the retarding phase substantially depleted of said second fraction to the said upper end of the first said passage.

6. A process as claimed in claim 1 in which substantially complete radial mixing of the forwarding phase is brought about repeatedly and within distances of flow not exceeding the order of magnitude of the passage diameter.

7. A process as claimed in claim 1, carried out in a substantially open, unpacked column, using the inner periphery of the column wall as the surface comprising the stationary retarding phase.

8. A process as claimed in claim 1 which comprises applying oscillations to the phases.

9. A process as claimed in claim 1, carried out with the retarding phase constituting the surface of particles at least 0.5 mm. in diameter.

10. A process as claimed in claim 1, carried out with a retarding phase applied to a support in a film thickness not exceeding 10^{-3} cm.

11. A chromatographic apparatus for carrying out chromatographic separations continuously and which comprises an upright column, adapted to contain a bed of particulate material comprising the retarding phase in a dense phase, expanded, non-turbulent, freeflowing condition, a bed support pervious to the forwarding phase and impervious to the retarding phase at the bottom of said column and an inlet for forwarding phase below the bed support, an outlet for forwarding phase containing a separated fraction above said bed support, intermediate between the bed support and said outlet for the forwarding phase an inlet for material to be separated, means for withdrawing particulate material from a locality below the inlet for the material to be fractionated, and means adapted to receive the particulate material thus withdrawn, removing therefrom a further separated fraction and returning the particulate material to the top of the said column.

12. The apparatus according to claim 11 wherein the means for withdrawing particulate material from the first column comprise a gate controlled downwardly directed passage leading into a second column having at its lower end an inlet for a transporting and stripping fluid, at its upper end a means for separating the particulate material from the transporting and stripping fluid, means for returning particulate material from said means for separating the particulate material to the top of the first-mentioned column and an outlet for the transporting and stripping fluid including the further separated fraction.

13. A pipeline for conveying fluid substances from one locality to another geographically different locality adapted as an essentially open tube chromatographic separating column and including inside the pipes of said

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pipeline formations adapted to induce turbulence inside the pipes, along the entire length thereof, taking the form of multiple repeated obstructions across the pipe interior on the surface of which is exposed a stationary retarding phase.

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