INDUSTRIAL SCALE CHROMATOGRAPHY

Usually only used when reaction optimization and non-chromatographic methods of purification are inadequate to prepare high purity product.

Procedure is time consuming due to:
• Requirement for column regeneration
• Large amount of in-process analysis
INDUSTRIAL SCALE HPLC

APPLIED TO HIGH VALUE POTENT COMPOUNDS

MAJOR ISSUES:
• SILICA SUPPORT IS EXPENSIVE
• SMALL THROUGHPUT - APPROX 1Kg / RUN
• COLUMN MUST BE WASHED TO REMOVE LATE ELUTING IMPURITIES AFTER EACH RUN
• LARGE VOLUMES OF SOLVENT ARE REQUIRED
• EXTENSIVE DISTILLATION AND/OR EXTRACTION REQUIRED BEFORE THE PRODUCT IS CRYSTALLISED

EXAMPLE:
RECOVERY OF VALUABLE API FROM MOTHER LIQUOR CONTAINING A RANGE OF IMPURITIES
ION EXCHANGE CHROMATOGRAPHY

COLUMN CONSISTS OF RESIN BEADS CONTAINING ACIDIC OR BASIC FUNCTIONAL GROUPS

• ACIDIC RESIN REMOVES BASIC IMPURITIES WITH GENERATION OF WATER
• BASIC RESIN REMOVES ACIDIC SPECIES WITH GENERATION OF WATER
• MIXED BED RESIN REMOVES SALTS FROM A RICH STREAM

• COLUMN MUST BE REGENERATED WITH ACID OR BASE AS APPROPRIATE AFTER USE

EXAMPLES:
• DEIONISATION OF WATER
• REMOVAL OF TRANSITION METAL CONTAMINANTS FROM A PROCESS STREAM
NEUTRAL RESINS

COLUMN CONSISTS OF NEUTRAL POLYMERIC RESIN BEADS WHICH SELECTIVELY ABSORB ORGANIC COMPOUNDS

OPERATING PRINCIPLE: ABSORPTION/DESORPTION

EXAMPLE: SEPARATE A WATER SOLUBLE ORGANIC COMPOUND FROM A SALT RICH AQUEOUS SOLUTION.

• PASS AQUEOUS SOLUTION DOWN RESIN COLUMN- ORGANIC COMPOUND IS SELECTIVELY ABSORBED AND SALT REMOVED WITH AQUEOUS STREAM

• ELUTE ORGANIC PRODUCT FROM THE RESIN WITH A SUITABLE ORGANIC SOLVENT AND ISOLATE BY CRYSTALLISATION

DISADVANTAGE: LARGE VOLUMES OF SOLVENT REQUIRED
CARTRIDGES

• RECENT INNOVATION (10 yr)

• CARTRIDGE CONTAINS ACTIVATED CARBON, SILICA etc.

• INSTALLED IN PROCESS LINE AND AVOIDS CONTAMINATION OF PROCESS EQUIPMENT WITH ABSORBENT MATERIAL

• PROCEDURE: PASS RICH SOLUTION THROUGH A SUITABLE CARTRIDGE WHICH WILL SELECTIVELY REMOVE AN IMPURITY.

• ISOLATE PRODUCT BY STANDARD PROCEDURES

• DISADVANTAGES: USUALLY ONLY APPLICABLE TO LOW LEVEL IMPURITIES AND MAY ABSORB SIGNIFICANT AMOUNTS OF PRODUCT