TITLE: PHENOTYPIC CHARACTERIZATION OF *Sphingomonas paucimobilis* AS A TRACKING TOOL FOR INVESTIGATION IN A PHARMACEUTICAL INDUSTRY

AUTORES: LAGE, R.V.S.; COSTA, L.V.; COSTA, P.V.; VASCONCELLOS, L.; SILVA, S.V.; REIS, C.M.F.; BRAGA, L.M.P.S.; MATTOSO, J.M.V.; SILVA, I.B.; BRANDÃO, M.L.L.

INSTITUIÇÃO: FUNDAÇÃO OSWALDO CRUZ, RIO DE JANEIRO, RJ (AV. BRASIL, 4365 - MANGUINHOS, CEP: 21040-900, RIO DE JANEIRO - RJ, BRASIL)

ABSTRACT:

Sphingomonas paucimobilis, a non-fermenting Gram-negative bacillus, is regarded as of minor clinical significance; however, many instances of infections with this organism can be found in the literature. Infections include bacteraemia/septicaemia caused by contaminated solutions, e.g. distilled water, haemodialysis fluid and sterile drug solutions. The objective of this study was to evaluate the phenotypic profile of *S. paucimobilis* strains as a tool for investigation in a pharmaceutical industry. *S. paucimobilis* (n=172) strains isolated from 2017-2021 were evaluated: 52 from purified water (PWI), 47 from bioburden assay of intermediate process solutions (IPS), 17 from environmental monitoring (EMO), 13 from process validation (PVA), 12 from intermediary or final products (IFP), nine from potable water (PTW), seven from water for injection (WFI), five from raw materials (RAM), five from cell cultures (CEC), three from active pharmaceutical ingredient (API), and two from reagents (REA). The strains were identified using the VITEK® 2 system with reliability ≥86%. The phenotypic profile was obtained from 47 biochemical tests and were categorized and evaluated with software Bionumerics 8.0 for similarity coefficient calculation using Pearson correlation and Unweighted Pair-Group Method using Arithmetic Avarages and minimum spanning tree (MST) algorithm. The profiles that presented similarity ≥85% were clustered in the same group. The Simpson`s index (SI) was applied to calculate the resolution power of VITEK® 2 for typing strains. The 172 strains were assigned in 155 phenotypic profiles and the calculated SI was 0.99. Similarity analysis showed 32 groups (I – XXXII) and 73 singletons. After MST analysis, the groups were assigned into 16 clusters according to the proximity between the nodes. The results indicate that PWI and EMO seems to be the mainly source of *S. paucimobilis* that further spreads throughout the production chain, contaminating WFI, IPS, IFA and IFP. In conclusion, the evaluation of the phenotypic profile of *S. paucimobilis* was considered an interesting tool for a fast and initial investigation in a pharmaceutical industry, since it revealed possible common sources of contamination. However, other genotyping methods as multi-locus sequence typing (MLST) are necessary to corroborate these results showing better resolution regarding the clonality origin of these strains.

Keywords: *Sphingomonas paucimobilis*, phenotypic characterization, Vitek® 2, pharmaceutical industry.

Development Agency: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).