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Master of Science HES-SO in Life Sciences

Physico-chemical compatibilities of drugs administered in Y at the HFR

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CHEMICAL DEVELOPMENT & PRODUCTION

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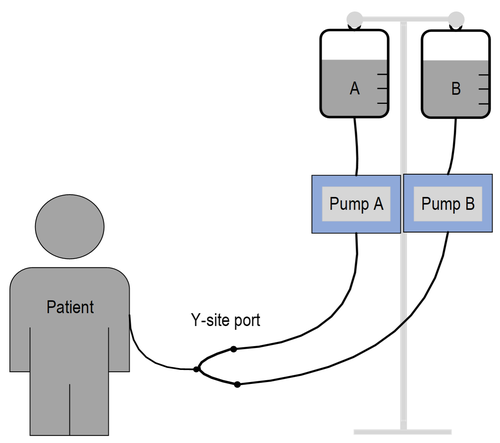
DESCRIPTION

Patients hospitalized in certain units of the HFR, such as the intensive care unit, generally require the administration of several drugs simultaneously. The most used mode of administration is intravenous, to be able to prescribe the drugs quickly and regulate the dosage rate.[1] However, intravenous access is limited and therefore leads via a Y-port.

The administration of intravenous treatments therefore requires control of physico-chemical parameters such as compatibility with the various diluents and product stability after dilution. The main diluents are glucose, sodium chloride or ringer lactate. This makes it possible to administer large volumes over a long period and to better control the dose administered. It is therefore equally important to ensure that the drug and the diluent are compatible, and that the two drugs are compatible with each other at the Y port site.[2] These administrations can be performed by two distinct venous routes venous routes: peripheral venous catheter (PVC) or central venous catheter (CVC).[3] The choice of administration of these two routes depends on various factors: drugs, duration of treatment, pH of the solution, osmolarity and concentration of the solution.

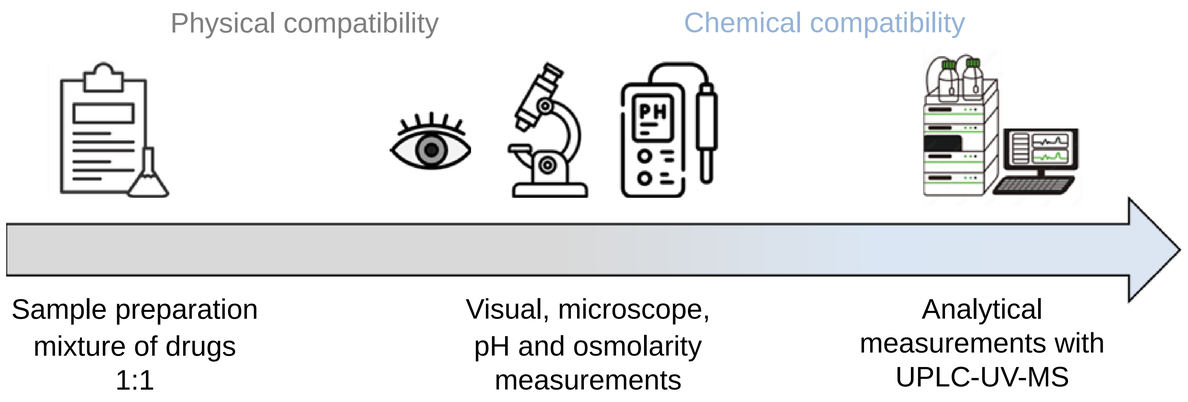


Example of Y administration

OBJECTIVES

The aim is to be able to respond to requests from nursing staff concerning the compatibility of the HFR. The results will be used to define whether there is compatibility and will be used to modify the administration sheets used daily by nursing staff.

Firstly, physical compatibility was studied to quickly determine any incompatibility. Physical compatibility measurements are also necessary so that subsequent administration protocols can be drawn up for nursing staff. Once physical compatibility has been assessed, it can be determined whether chemical compatibility needs to be studied. It is then necessary to check quantitatively by LC-MS whether 2 drugs administered in Y are compatible. For all tests, measurements were carried out at time 0h and time 4h to ensure mixture stability over time. The figure describes the strategy used to assess the compatibility of mixtures for Y administration.



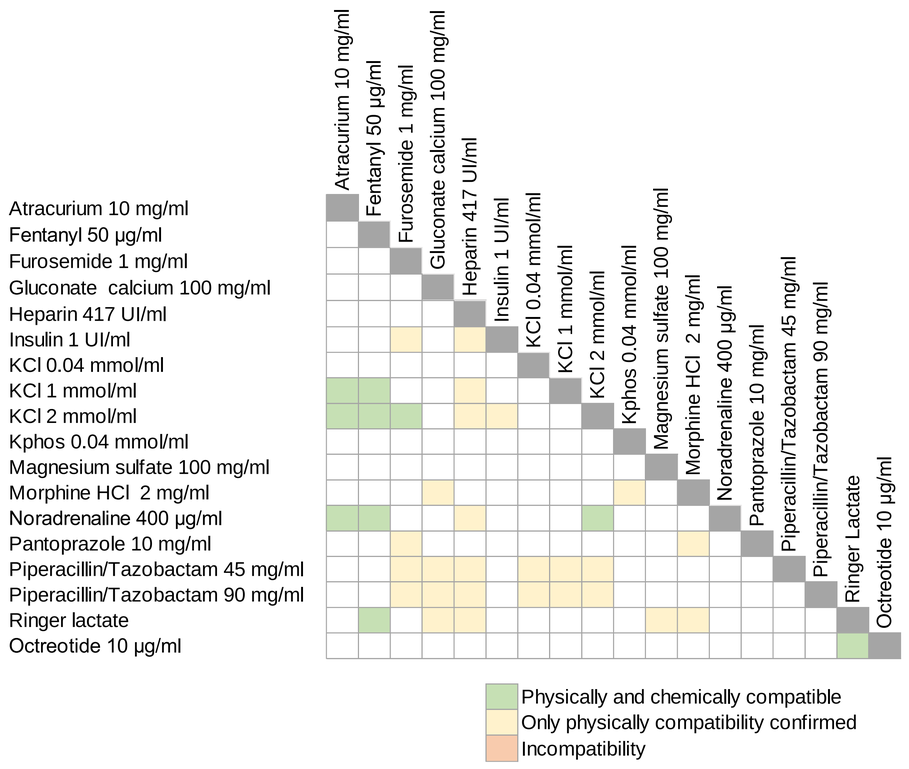
Strategy to determine the compatibility of mixtures for Y administration

RESULTS

All the physical compatibilities were validated by measurements of drug mixtures at t0h and t4h. These measurements consisted of a visual observation and measurements of pH, osmolarity and particles under the microscope. This method to measure particles proved difficult to interpret and unrepresentable because only one drop of the mixture was analysed. For a more detailed measurement, a particle counter should be used. This measurement is not essential to determine whether there is any incompatibility.

Chemical compatibility methods were developed for furosemide, atracurium, noradrenaline, fentanyl, piperacillin/tazobactam, octreotide and pantoprazole. However, challenges were encountered during sample preparation, particularly for the analysis of furosemide with pantoprazole and fentanyl with salts such as KCl or ringer lactate. The chemical compatibility of pantoprazole could not be assessed, and adjustments were required for the preparation of fentanyl samples without impacting on the analysis itself.

Certain compounds such as heparin or calcium gluconate, for example, can be very polar and therefore require very specific UPLC columns in to be retained. The analysis of insulin, which is a protein, is complicated by its size and structure. However, a method for analysing morphine could easily be set up, as it is an alkaloid like noradrenaline. The same eluents could be used and the advantage is that morphine is much less polar than noradrenaline, so a C18 UPLC column could be used. In this work, a phenyl hexyl HPLC column had to be used to analyse noradrenaline to retain the compound. It would have been preferable to use a UPLC type column to avoid the problems associated with MS module. In fact, the flow rate had to be adjusted to 1ml/min, but the mobile phase contains 98% water, this poses a certain difficulty for the MS in evaporating the solvent. This method is therefore feasible but not optimal. In the case of piperacillin/tazobactam, the analysis method was developed so that both components could be quantified simultaneously. However, the UPLC lamp was faulty, so samples containing these drugs could not be run. Once this problem has been resolved, these compatibilities can be studied rapidly. For mixtures containing heparin, insulin, calcium gluconate, morphine and piperacillin/tazobactam only physical compatibility has been studied.



Compatibility table completed according to analysis results

CONCLUSION

The results obtained for physical compatibility already provide crucial information on the stability of medicinal mixtures. For a more complete assessment, the integration of chemical compatibility data is essential. Visual observations, pH and osmolarity measurements and particles analysis provide relevant indicators, but understanding the chemical interactions between components is necessary to ensure the integrity of pharmaceutical preparations. The technical challenges encountered in chemical analysis underline the importance of being able to identify the source of incompatibility to ensure reliable results. By combining aspects of physical and chemical compatibility, nursing staff can make informed decisions, boosting confidence in the use of the medicinal mixtures studied.

[1] V. B. T.-T. in the B. and N. S. Claassen, Ed. , in Neglected Factors Pharmacol. Neurosci. Res., Elsevier, **1994**.
[2] V. Humbert-Delaloye, *Administration Des Médicaments Par Voie Intraveineuse Aux Soins Intensifs Adultes : Évaluation et Validation Des Pratiques Par La Littérature et Des Essais En Laboratoire*, **2012**.
[3] L. Piquard, “Cathéters Midline et PiCCline : des indications différentes,” can be found under actusoins.com/315932/catheters-midline-et-piccline-des-indications- differentes.html, **2019.**