OPTIMIZATION OF THE SPECTROPHOTOMETRIC QUANTITATIVE ANALYSIS METHOD OF DICLOFENAC SODIUM DRUG SUBSTANCE

Saburov I.K. Yunuskhodjayeva N.A.
Tashkent Pharmaceutical institute, Tashkent, Republic of Uzbekistan.
e-mail: iundch@mail.ru, mobile: (91) 191-12-39

The purpose of the study: Development and optimization of effective methods for the determination of active pharmaceutical substances as foreign substances in MACO quantities in the production processes of pharmaceuticals Development of an optimized spectrophotometric quantitative analysis method for the Diclofenac sodium drug substance for validation of purification processes.

Methods of the research: ultraviolet spectrophotometric method of analysis, and below materials which were used during this study:

- 1, 2 ml and 5 ml volume graduated measuring pipettes;
- 5, 10, 25 ml and 50 ml volumetric flasks;
- Purified water, 96% ethanol solution;
- Drying oven;
- Analytical balance;
- A working standard sample of the drug substance Diclofenac sodium;
- spectrophotometer-UV1900.

Results of the research: Diclofenac sodium is produced in the form of solutions with a concentration of 10 mg/ml. However, when calculating the MACO (Maximum Allowable Carryover - Maximum Allowable Carryover) for the validation of cleaning processes, a total amount of 9 µg was determined, and this is the amount of Diclofenac sodium that should be determined from each sample taken, when distributed over all production equipment surfaces and cleanroom work surfaces. was 4.5 ng. After determining the target concentration, based on the solubility properties of the Diclofenac sodium drug substance (very easily soluble in aqueous solutions of water and acids, soluble in alcohol solutions) and other physico-chemical properties, samples of Diclofenac sodium with an amount of 4.5 ng/ml in 3 different solvents (in purified water, in 0,1M hydrochloric acid solution and 96% ethyl alcohol solution) were prepared and their spectrum in the ultraviolet region was obtained. Absorbance levels (abs-absorbance) of the solutions were determined at the identified absorption maxima. The results are presented below:

Solvent 1 (purified water): the absorption maximum was 253nm wavelength, the absorption level was 0.124abs;

Solvent 2 (in 0.1M hydrochloric acid solution): the absorption maximum was at 338nm and 273nm wavelength, the absorption level was 0.195-0.199abs;

Solvent 3 (90% ethyl alcohol solution): absorption maximum at 362nm wavelength, absorption level was 0.598abs.

Taking into account the results and the fact that the most optimal absorption level in spectrophotometric analysis methods are solutions with a concentration in the range of 0.4-0.8abs, solvent 3 was selected for the development of the analysis method. At the next stage, the validation of the analysis method was carried out in accordance with the requirements of the ICH (International Council for Harmonization - International Consulate for Coordination of Requirements in the Pharmaceutical Industry) guidelines, and indicators such as the specificity of the method, the limit of detection and the limits of quantitative analysis were evaluated.

Conclusion: the developed analysis method fully complied with the validation requirements of international guidelines, its specificity, detection and quantitative analysis limits were confirmed. It was recommended to use the created method to determine residual amounts of Diclofenac sodium as a foreign substance in the further validation of purification processes.

Bibliography

1. British Pharmacopeia. Edition 2022.
2. РУКОВОДСТВО по валидации аналитических методик: Евразийской экономической комиссии.

3. Йоахим эрмер, Джон Х. МакБ. Миллер «Валидация методик в фармацевтическом анализе», Перевод с английского языка под редакцией Александрова А.В. Москва, 2013.
4. Н.А. Юнусходжаева, К.А.Убайдуллаев. Разработка и валидация методики количественного определения суммы флавоноидов жидкого экстракта “Гемоста”.//Фармацевтический журнал. 2017.-№1.-С.29-33
5. United States Pharmacopoeia/ Validation of compendia methods. USP26-NF21.2003.
6. «Чистые помещение и технологические среды» научно – практический журнал, №1, январ-март 2018
7. Государственная фармакопея Российской федерации XIII издания.
8. Эрмер Йоахим, Миллер Джон. Валидация методик в фармацевтическом анализе. Примеры наилучшей практики. Пер. с англ. — М.: Группа компаний Виалек, -2013. - 512 с
9. Руководство ICH – Q3A-Q3E. Примеси. 2006 год, 5 стр.
10. «Зарур ишлаб чиқариш амалиёти» O’z DSt 2766:2018. 2018-йил, 13-илова., квалификация ва валидация. 160-165 бетлар.
11. GUIDANCE ON ASPECTS OF CLEANING VALIDATION IN ACTIVE PHARMACEUTICAL INGREDIENT PLANTS. APIC 2016. 54-55 pages.
12. WHO Technical Report series № 937. WHO expert committee on specifications for pharmaceutical preparations. Fortieth Report. Geneva, 2006. Annex 4 “Supplementary guidelines on good manufacturing practices: validation”, Appendix 3 “Cleaning Validation” 127-135 бетлар.
13. WHO Supplementary Training Modules. Cleaning Validation, John Startup, February 23-27, 2009, Uganda.
14. Cleaning Validation in the Pharmaceutical Industry. By Mowafak Nassani, PhD. 48-49 бетлар.
15. Guide to Inspections Validation of Cleaning Processes”, US-FDA, 2004.
16. Cleaning Validation: Defining Limits and Doing MACO Calculations. Pierre Devaux. ACM Pharma, France, 12-20 бетлар.
17. PDA. Technical Report No. 29 (Revised 2012). Points to Consider for Cleaning Validation, 29-34 бетлар