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Analysis of the testing capability and actual requirements: a case study at the Da Nang Quality Control Center in 2021

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Abstract

The quality evaluation of drugs necessitates the utilization of suitable methodologies, tools, and equipment. However, the continuous progress in the pharmaceutical sector has resulted in a wide range of diverse products, presenting a formidable challenge for drug testing centers. This study aimed to analyze the testing capacity and actual analysis requirements at the Da Nang Quality Control Center (DQCC) in Vietnam. A descriptive cross-sectional study design was employed, and testing records of DQCC in 2021 were retrieved for analysis. The findings revealed limitations and challenges faced by DQCC in testing tablets, injectable drugs, and medicinal herbs. Equipment shortages, lack of standardized materials, and insufficient availability of chemicals were identified as major obstacles. Consequently, 19.77% of required tests for tablets could not be conducted. Injectable drugs posed greater difficulties, with crucial tests like clarity, sterility, and pyrogen presence not being performed on any samples. Testing capacity for medicinal herbs was significantly limited, with only 15.46% of samples being examined, primarily due to equipment shortages, lack of necessary chemicals and standards. These limitations are not exclusive to DQCC but are prevalent in other testing centers as well. The study highlights the need for attention and investment from higher-level organizations to overcome these challenges. By addressing equipment shortages, providing standardized materials and chemicals, and enhancing the overall testing infrastructure, DQCC can improve its capabilities, adhere to international standards, and ensure the quality of pharmaceutical products. Future research should focus on improving testing capacity for tablets, injections, and herbal/traditional drugs to meet the increasingly strict requirements and variety of dosage forms of the pharmaceutical sector.

Keywords: Drug Quality Control Center, drug testing capability, analysis capability, drug quality evaluation, analysis requirements.

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Tóm tắt

Việc đánh giá chất lượng thuốc đòi hỏi phải sử dụng các phương pháp, công cụ và thiết bị phù hợp. Tuy nhiên, sự tiến bộ không ngừng trong lĩnh vực dược phẩm đã dẫn đến một loạt các sản phẩm đa dạng, tạo ra một thách thức lớn cho các trung tâm kiểm nghiệm thuốc. Nghiên cứu này nhằm phân tích năng lực thử nghiệm và yêu cầu phân tích thực tế tại Trung tâm Kiểm nghiệm Đà Nẵng (DQCC) tại Việt Nam. Nghiên cứu sử dụng thiết kế cắt ngang mô tả, hồi cứu các hồ sơ thử nghiệm của DQCC vào năm 2021 để truy xuất dữ liệu và phân tích. Kết quả cho thấy những hạn chế và thách thức mà DQCC phải đối mặt trong việc thử nghiệm thuốc viên, thuốc tiêm và dược liệu. Tình trạng thiếu thiết bị, thiếu vật liệu tiêu chuẩn hóa và không đủ hóa chất được xác định là những trở ngại lớn. Do đó, 19,77% số chỉ tiêu kiểm tra bắt buộc đối với dạng viên nén đã không thể thực hiện. Các loại thuốc tiêm gặp nhiều khó khăn hơn, với các phép thử quan trọng như độ trong, độ vô khuẩn và chất gây sốt không được triển khai. Năng lực kiểm nghiệm dược liệu còn hạn chế, chỉ có 15,46% số mẫu được kiểm nghiệm, chủ yếu do thiếu trang thiết bị, thiếu các hóa chất, chất chuẩn cần thiết. Nghiên cứu đã chỉ ra sự cần thiết của việc quan tâm và đầu tư từ các tổ chức cấp trên để vượt qua những thách thức này. Bằng cách giải quyết tình trạng thiếu thiết bị, cung cấp vật liệu và hóa chất tiêu chuẩn hóa, đồng thời tăng cường cơ sở hạ tầng thử nghiệm tổng thể, DQCC có thể nâng cao năng lực của mình, tuân thủ các tiêu chuẩn quốc tế và đảm bảo chất lượng dược phẩm. Nghiên cứu trong tương lai nên tập trung vào việc cải thiện năng lực kiểm nghiệm đối với thuốc viên, thuốc tiêm và thuốc dược liệu, thuốc cổ truyền nhằm đáp ứng yêu cầu ngày càng khắt khe và sự đa dạng về bào chế của ngành dược phẩm.

Từ khóa: Trung tâm kiểm nghiệm, năng lực kiểm nghiệm, năng lực phân tích, đánh giá chất lượng thuốc, yêu cầu phân tích.

1. Introduction

In order to assess the quality of drugs, it is crucial to employ suitable methodologies, tools, and equipment. The responsibility for conducting such evaluations lies with competent regulatory agencies, necessitating the presence of skilled and knowledgeable examiners [1]. Conversely, the continual advancements in science and technology have facilitated remarkable progress within the pharmaceutical industry, resulting in a diverse array of drugs encompassing various formulations and designs. Consequently, this presents a formidable challenge for the drug testing sector, which must contend with the arduous task of monitoring, testing, and ensuring quality assurance for these evolving pharmaceutical services.

Recent research on the rankings of Drug Quality Control Centers across the country revealed that only one Center has been rated as Good/Very Good, while the remaining Centers have received lower rank [4]. Therefore, it is imperative to allocate increased attention and investment to local drug testing laboratories, not only in Da Nang city but also in numerous other Centers nationwide. This step is essential to ensure the effective operation of the quality management system, in compliance with the regulations outlined in the Pharmacy Law and its associated guidelines [3, 6].

The Da Nang Drug Quality Control Center (DQCC) operates as an official drug testing facility under the government's purview. DQCC assumes a crucial role as an advisory body to the Department of Health and is responsible for the comprehensive testing and monitoring of drug quality throughout the city. As per Article 104 of the Pharmacy Law, state-owned drug quality control centers are additionally entrusted with providing suggestion to relevant government agencies within the Ministry of Health regarding technical measures aimed at strengthening appropriate drug quality management, in accordance with the prevailing socio-economic conditions [3]. Consequently, in order to enhance the analytical capabilities of DQCC, maintain compliance with ISO/IEC 17025 standards, and progress towards implementing Good Laboratory Practices (GLP), thorough analysis of the underlying factors contributing to the incapacity to conduct essential tests for quality control activities must be undertaken [7]. Factors such as inadequate

equipment, facilities, chemicals, and reference standards may all contribute to this situation.

2. Materials and methods

Materials: File retrieval all testing records, including: certificates of analysis, analytical profiles, testing records of DQCC in the year of 2021.

Methods: Descriptive cross-sectional study was designed.

3. Results

In 2021, the DQCC demonstrated utmost dedication to fulfilling its assigned task and successfully tested a total of 763 samples. The results obtained from these tests provide valuable insights into the quality of drugs circulating within the city. DQCC prioritized the testing of tablet samples, which largest proportion of the overall samples examined, specifically 44.30% (Table 1). In contrast, number of samples for injection drug testing is minimal, only 0.79%. Among the samples examined, a concerning finding emerged, indicating that 4.46% of the drug samples were substandard. In which, it is worth noting that the number of herbal and traditional drugs was detected with 19 samples, accounting for more than half of the total number of substandard drugs of 34 samples. Therefore, the capability of testing tablets, injections and herbal/traditional drugs is of interest to be included in our next research steps.

Table 1. Test results, categorized by dosage forms

No	Drug dosage forms	Passed		Not passed		Total	Percentage (%) / Grand total
		Number	Percentage (%)	Number	Percentage (%)		
1	Tablets	329	43.12	09	1.18	338	44.30
2	Capsules	185	24.25	02	0.26	187	24.51
3	Pills	08	1.05	-	-	08	1.05
4	Powder	61	7.99	01	0.13	62	8.13
5	Ophthalmic/nasal drops	13	1.70	-	-	13	1.70
6	Injections/parenteral preparation	06	0.79	-	-	06	0.79
7	Solutions, oral liquid form	28	3.67	03	0.39	31	4.06
8	Herbal/traditional drugs	99	12.97	19	2.49	118	15.46
	Total	**729**	**95.54**	**34**	**4.46**	**763**	**100**

In practice, DQCC diligently executed tests pertaining to the properties, as listed in Table 2. For qualitative tests, DQCC employed High-performance liquid chromatography (HPLC) and chemical identification, successfully completing 100% and 83.33% of the samples, respectively (Table 3). Only 16.67% of the samples were excluded from the qualitative chemical test. Out of the 50 samples necessitating qualitative testing using the Thin-layer chromatography (TLC) method, DQCC successfully tested 39 samples (account for 78.00%). In terms of quantitative tests, DQCC conducted 100% of UV-Vis measurement, antibiotics-microbial assay (Table 4). Notably, 3 samples (accounted for 1.82%) of HPLC assay tests, and only one sample of volumetric titPercentagen test could not be subjected to be conducted as required quantitative methods by specifications.

Table 2. Comparison of tested specification with the required test item for tablet dosage forms

No.	Specifications		Number of sample	Tested		Not tested	
				Number	Percentage (%)	Number	Percentage (%)
1	DisintegPercentagen		211	211	100	-	-
2	Uniformity of weight		312	312	100	-	-
3	Uniformity of content		26	26	100	-	-
4	Moisture	Karl Fischer	09	09	100	-	-
		Distilled method	14	14	100	-	-
		Loss on drying	35	30	85.71	5	14.29
5	Dissolution		127	127	100	-	-
6	Related substances		117	54	46.15	63	53.85
7	Determination of optical rotation and specific rotation		05	05	100	-	-

Table 3. Comparison of tested qualitative method with the requirements for tablet dosage forms

No.	Qualitative method	Number of sample	Tested		Not tested	
			Number	Percentage (%)	Number	Percentage (%)
1	Chemical identification	48	40	83.33	8	16.67
2	HPLC identification	165	165	100	-	-
3	TLC identification	50	39	78.00	11	22.00
4	UV-Vis identification	75	75	100	-	-
	Total	**338**	**319**	**94.38**	**19**	**5.62**

Table 4. Comparison of tested quantitative method performed with the requirements for tablet dosage forms

No.	Quantitative method	Number of sample	Tested		Not tested	
			Number	Percentage (%)	Number	Percentage (%)
1	HPLC assay	165	162	98.18	3	1.82
2	Volumetric titration	21	20	95.24	1	4.76
3	UV-Vis assay	127	127	100	-	-
4	Antibiotics-microbial assay	25	25	100	-	-
	Total	**338**	**334**	**98.82**	**4**	**1.18**

Regarding the capacity for tablet testing, DQCC was able to conduct tests comprehensively on fundamental requirements of Vietnam Pharmacopoeia V (VP-V). However, DQCC encountered challenges in performing 86 tablet tests, which accounted for 19.77% of the total. Among these, 39.53% were attributed to equipment shortages,

39.53% to the lack of standardized materials, and 40.70% due to insufficient availability of chemicals (Table 5).

Table 5. Capability-related reasons for not tested item on the tablet dosage form

No.	Test item	Number of sample	Lack of equipment		Lack of standard compound		Lack of chemical, reagent	
			Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)
1	Chemical identification	8	-	-	-	-	8	100
2	TLC identification	11	-	-	2	18.18	9	81.82
3	Related substances	63	16	25.40	32	50.79	15	23.81
4	HPLC assay	3	-	-	-	-	3	100
5	Volumetric titration assay	1	1	100	-	-	-	-
	Total	**86**	**17**	**19.77**	**34**	**39.53**	**35**	**40.70**

DQCC conducted a number of tests on these samples, as described specifically in Table 6. However, DQCC has not yet performed tests for clarity, sterility, and pyrogen presence on the samples designated for these specific evaluations.

Table 6: Comparison of tested specification with the required test item for parenteral dosage forms

No.	Specifications	Number of sample	Tested		Not tested	
			Number	Percentage (%)	Number	Percentage (%)
1	pH value	6	6	100	-	-
2	HPLC assay	5	5	100	-	-
3	Antibiotics-microbial assay	1	1	100	-	-
4	Sterility	6	-	-	6	100
5	Clarity of solution	6	-	-	6	100
6	Microbial limits	6	6	100	-	-
7	Uniformity of volume	6	6	100	-	-
8	Bacterial endotoxins	6	6	100	-	-
9	Test for Pyrogen	6	-	-	6	100

Those data showed that the capability to test injectable and intravenous drug samples remains limited. Crucial tests such as clarity, sterility, and pyrogen presence have yet to be executed on any of the samples. In the case of injectable forms, the inability to conduct 100% of the required tests can be attributed solely to equipment and tool shortages (Table 7). The stringent conditions necessary for these tests, such as sterile chambers, clean rooms, and laboratory animal facilities, demand substantial financial resources beyond DQCC authority. Consequently, DQCC requires the attention of upper level organizations to allocate appropriate funding.

Table 7. Capability-related reasons for not tested item on the parenteral dosage form

No.	Test item	Number of sample	Lack of equipment		Lack of standard compound		Lack of chemical, reagent	
			Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)
1	Test for Pyrogen	6	6	100	-	-	-	-
2	Sterility	6	6	100	-	-	-	-
3	Clarity of solution	6	6	100	-	-	-	-

DQCC received and examined a total of 118 samples of medicinal herbs/traditional drugs. In practice, DQCC only conducted several tests on the examined herbal samples, as described specifically in Table 8. Among these, 57 samples of medicinal herbs were chemical identified, constituting 87.69% of the tested samples, while 8 samples remained unidentified due to a lack of necessary chemicals. Furthermore, 15 samples of medicinal herbs, amounting to 28.30%, were unable to undergo testing through the TLC method. DQCC was unable to carry out 33 out of 48 quantitative tests (68.75%) for medicinal herbs. None of the transverse section microscopy was conducted on the herbal samples.

Table 8: Comparison of tested specification with the required test item for herbal/traditional drugs

No.	Specifications		Number of sample	Tested		Not tested	
				Number	Percentage (%)	Number	Percentage (%)
1	Powder microscopy		118	118	100	-	-
2	Transverse section microscopy		12	-	-	12	100
3	Ash	Total ash	77	77	100	-	-
		Acid-insoluble ash	41	41	100	-	-
4	Moisture	Solvent distillation	31	31	100	-	-
		Loss on drying	74	74	100	-	-
5	Assay of extractives	Cold extraction	59	59	100	-	-
		Hot extraction	22	22	100	-	-
6	Identification	Chemical	65	57	87.69	8	12.31
		TLC	53	38	71.70	15	28.30
7	Impurities		118	118	100	-	-
8	Assay		48	15	31.25	33	68.75

Regarding the testing capacity for medicinal herbs, DQCC was able to examine only 15.46% of the total samples (Table 1). The inability to conduct tests on the remaining herbal samples was primarily attributed to equipment shortages, which accounted for 100% of the cases mainly due to the absence of kits for transverse section microscopy and high-performance liquid chromatography instruments (Table 9). The qualitative analysis through TLC could not be performed due to a lack of chemical standards and reagents (40%). Similarly, quantitative tests could not be carried out due to the unavailability of storage kits for medicinal herbs (6.06%), reference standards (63.64%), and chemicals (30.30%).

Table 9. Capability-related reasons for not tested item on the parenteral dosage form

No.	Test item	Number of sample	Lack of equipment		Lack of standard compound		Lack of chemical, reagent	
			Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)
1	Transverse section microscopy	12	12	100	-	-	-	-
2	Chemical identification	8	-	-	-	-	8	100
3	TLC identification	15	-	-	9	60	6	40
4	Assay	33	2	6.06	21	63.64	10	30.30
	Total	**68**	**14**	**20.59**	**30**	**44.12**	**24**	**35.29**

4. Disussions

The results obtained shed light on the testing and analytical capacity of DQCC in 2021, in the context of the sampling process facing many challenges due to the impact of the COVID-19 pandemic. Despite these obstacles, the DQCC demonstrated a strong commitment to fulfilling its responsibilities in assessing drug quality. A total of 763 samples were successfully tested, providing valuable insights into the quality of drugs circulating within the city.

The analysis of the samples revealed some concerning findings. Among the tested samples, it was observed that a significant proportion (4.46%) did not meet the required standards, indicating substandard drug quality (Table 1). Notably, herbal and traditional drugs accounted for more than half of the substandard drugs, with 19 out of 34 samples falling into this category. This highlights the importance of improving testing capability on herbal/traditional drugs as recommended by World Health Organization (WHO) [8].

The study also evaluated the testing capabilities of DQCC based on various dosage forms. In terms of qualitative tests, the center achieved a high success rate, with 100% completion for HPLC-based tests and 83.33% completion for chemical identification. However, some samples (16.67%) were excluded from the qualitative chemical test (Table 3). For quantitative tests, DQCC successfully conducted UV-Vis measurements and antibiotics-microbial assays for all samples. However, a small percentage (1.82%) of HPLC assay tests and only one sample of volumetric titration test could not be performed as required (Table 4). The above results have shown both the advantages and limitations of DQCC's testing capacity, and are similar to many other testing centers across the country [4].

The capacity for tablet testing was generally satisfactory, with comprehensive testing conducted for the fundamental requirements of VP-V [2]. However, DQCC encountered challenges in performing certain tablet tests, primarily due to equipment shortages, the lack of standardized materials, and insufficient availability of chemicals. These factors collectively accounted for a significant portion (19.77%) of the tests that could not be conducted (Table 5). In the case of injectable forms, the testing capacity of DQCC remained limited. Essential tests such as clarity, sterility, and pyrogen were not executed for any of the samples. The main reason for this limitation was the lack of necessary equipment and tools, which require substantial financial resources beyond the authority of DQCC (Table 7). This

result shows that there are still many gaps that need to be filled in the testing capacity of DQCC in the development trend with many scientific advances in drug analysis and quality control [1, 5] and for maintaining laboratory accreditation [7]. Therefore, addressing these resource constraints necessitates the attention and support of higher-level organizations to allocate appropriate funding.

For medicinal herbs and traditional drugs, the testing capacity of DQCC was found to be relatively low. Only a small percentage (15.46%) of the total samples were examined (Table 1), primarily due to equipment shortages, the lack of necessary chemical standards and reagents, and the unavailability of storage instruments, reference standards, and chemicals. These constraints prevented the execution of qualitative and quantitative tests as required by technical guidance and recommended by WHO [2, 3, 8].

5. Conclusions

In conclusion, the results indicate that while the DQCC has made commendable efforts in testing drug samples, there are notable areas for improvement, particularly in the testing of tablets, injections, and herbal/traditional drugs. Addressing the underlying factors contributing to the incapacity to conduct essential tests, such as equipment shortages, lack of standardized materials, and insufficient availability of chemicals, is crucial for enhancing the analytical capabilities of DQCC and ensuring compliance with quality standards. Moreover, adequate support and funding from higher-level organizations are necessary to overcome the resource limitations faced by the center.

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