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Article

# A framework for advanced technology medicines from the perspective of community pharmacists; with or without technology

**Merve Memisoglu[1*], Ömer Bilen[2]**

*[1]Department of Social Pharmacy, Biruni University, Istanbul, Turkey, [2]Department of Urban and Regional Planning, Bursa Technical University, Bursa, Turkey*

Nowadays, the number of medicines manufactured using advanced technologies such as biotechnology, nanotechnology, and 3D printing is increasing along with the accelerated pace of technological change. Evaluating high technology medicines from the perspective of community pharmacists is important for the quality of the pharmacy practice. The aim is to analyze the knowledge, attitude, and behavior of community pharmacists regarding advanced technology medicines and to examine the social and ethical aspects from the pharmacist's perspective. A face-to-face cross-sectional survey was conducted with each of the 879 community pharmacists in Istanbul using a stratified sampling method. In this context, the gaps in pharmacists' knowledge of high technology medicines were determined. It has been found that the pharmacists' level of knowledge and willingness to learn new technologies differs according to the current education levels of the pharmacists and diversity in patient profiles. The pharmacists should close the knowledge gaps and update their information about medicines that are manufactured via the implementation of advanced technologies. The more pharmacists adapt to technology, the better guidance they can offer to society. This will also ensure that communication between the pharmacist and the patient to be built on trust, and significantly improve pharmacy practice.

**Keywords:** Advanced technology medicines. Nanomedicines. Biologic drugs. 3D-printed drugs. Community pharmacists.

## INTRODUCTION

Technology, encountered at every point of our daily lives, has inevitably influenced and transformed the pharmaceutical industry. In today's world, where even supposedly new technology swiftly gets old, only those professions that can adapt to this rapid change will remain relevant. A recent example of this is the transition of the school education system to the EdTech system, including online learning, as a result of the global COVID-19 pandemic that we are currently experiencing. Digital transformation is inevitable in every sphere of life, for all of us.

Whether pharmacists can keep up with Industry 4.0, which is bringing reforms such as artificial intelligence, the Internet of Things (IoT) and other new technologies, will be very important for the future of pharmaceutical services. These technologies are now being used in pharmacies for many purposes, such as increasing the medication adherence of patients and monitoring stock levels (Baines, Nørgaard, Rossing, 2020). However, technological developments in the pharmaceutical area are not limited to pharmacy practice but also apply to the manufacturing of medicines which is one of the most important pillars of the pharmaceutical practice.

The aim of our study is to examine the knowledge, attitudes and behaviors of community pharmacists with regard to high technology drugs, including ethical and social dimensions. Among the advanced technology products included in the study are nanomedicines,

***Correspondence:** M. MemisogluDepartment of Social Pharmacy. Faculty of Pharmacy Biruni University 10. Yıl Caddesi, Protokol Yolu No: 45 34010 Topkapı, Istanbul, Turkey. E-mail: mmerve.memisoglu@gmail.com. ORCID: https://orcid.org/0000-0002-8068-6836

biotechnological drugs (including reference biologics, biosimilars), and 3D-printed drugs.

Nanotechnology concerns extremely small structures called nano-sized particles (from 0.1nm to 100nm), breaking ground in healthcare as well as in other fields (Garnett, Kallinteri, 2006). Some people hold the opinion that nanomedicines are completely safe. Accordingly, it was found that Italian citizens approach nanomedicines positively although they do not have clear information on nanomedicines (Bottini *et al.,* 2011). Pharmacists receive information on the pharmaceutical applications of nanotechnology during their undergraduate education, but there is no research on the experience of pharmacists with these products in practice. How much do pharmacists know about the concept of nano-divide, which paves the way for social injustice as an ethical problem in nanotechnology (Maclurcan, 2009)? How aware are the pharmacists of the possible toxic effects of nanomaterials (Timmermans, Zhao, van den Hoven, 2011)? In a study conducted among hospital pharmacists in Palestine, it was found that their knowledge of nanomedicines was limited (Assali *et al.,* 2018). In our study, the knowledge of pharmacists about nanotechnology-based products and the ethical dimension of nanotechnology were examined from the pharmacist's perspective.

Another product group to be examined within the scope of this study is biotechnology-based products.

While nanotechnology-based medicines are ultra-small, biotechnology involves very large and complex structures and uses biological systems, living organisms, or derivatives thereof. It is essential for healthcare professionals to know that biosimilars are not identical to the reference biological product, unlike generics. A survey on biosimilars conducted by The Biosimilars Forum revealed the concern of physicians who prescribe these medicines arising from the knowledge gap and lack of confidence, emphasizing the need for evidence-based education (Cohen *et al.,* 2016). The research of European Society for Medical Oncology (ESMO) into physicians shows that there are differences between the European and Asian Pacific regions, and there is a lack of knowledge and need for education of physicians, especially in the development of biosimilars, trial design and extrapolation of indications (Giuliani *et al.,* 2019).

Similarly, in the review by Leonard et al., covering data from 2014-2017, the gaps in the education of healthcare providers was emphasized and it was reported that education of health care providers would decrease safety and efficacy concerns and increase biosimilar prescribing (Leonard *et al.,* 2019). In a study conducted among pharmacists in France, it was found that they were able to distinguish between biosimilars and generic drugs and that they had sufficient information about biosimilars. It was stated that the responsibility for immunogenicity risk management should be shared by the physician and the pharmacist, and interchangeability could be possible by obtaining the informed consent of the patient (Adé, Bourdon, Bussières, 2017). In another study conducted among hospital pharmacists, 88% of the participants expressed concerns that biosimilars differ from reference biologic products in terms of immunogenicity and pharmacokinetic profile. However, it was observed that they were aware of the cost-effectiveness as an advantage, but were not willing to substitute without a doctor's permission (Pawłowska *et al.,* 2019). The question raised at this point is whether the pharmacist can give a biosimilar instead of a reference biologic. In our study, this issue has been examined from the pharmacist's perspective.

There have been studies conducted on pharmacovigilance associated with biopharmaceuticals. Risk management and biologic post-market safety surveillance are essential for patient safety. Most healthcare professionals stated that they indicate the brand name when reporting adverse reactions, and although they were aware of the importance of notifying the batch number, they found it to be a difficult process. In general, they were found to be more familiar with biological medicines than biosimilars. In the same study, pharmacists were found to have the highest awareness of the black triangle symbol as the requirement for additional monitoring among all healthcare professionals (O'Callaghan *et al.,* 2018). Pharmacists' perspective on the safety of biopharmaceuticals is another issue explored in our study.

In the scope of our research, the 3D printing of medicines stands out as another advanced technology production. Complex products, especially those that support personalized therapy and personalized drug dosing, can be produced with 3D printing, thereby increasing patient medication adherence and preventing possible complications of polypharmacy (Alomari *et al.,* 2015; Norman *et al.,* 2017). Patient-oriented research continues into drug manufacturing with 3D printing in pharmacies (Aquino *et al.,* 2018). It seems that the production by the pharmaceutical industry of drug-loaded filaments of sufficient quality and safety to meet GMP requirements can make personalized medicine production possible by the pharmacist in the pharmacy with 3D printing using these filaments (Araújo *et al.,* 2019). How ready are community pharmacists for such a transformation? In addition, disadvantages in 3D printing production (such as API degradation by temperature) are challenges that must be overcome (Alhnan *et al.,* 2016). How aware are pharmacists of these problems? Finding answers to these questions is another focus of our research. The results obtained from our study will serve as a reference, since a cross-sectional analysis in this context (nanotechnology, biotechnology, 3D printing, etc.) was conducted among community pharmacists for the first time.

## METHODS

### Study Design and Population

A cross-sectional study was conducted in Istanbul. Istanbul, which is one of the world's largest cities, is divided into 40 districts in 2 geographical regions – the European and Asian sides. Each subgroup was weighted according to its respectiveshare of the main population. Thus, all subgroups were equally represented in the sample.

Accordingly, the sample was calculated as n=879 (margin of error: ±3.00%). The pharmacies were randomly selected by stratified sampling based on the population of the district and a face-to-face interview with the pharmacists was conducted. If a pharmacist was not available, the survey was conducted in the nearest pharmacy to make up a sufficient number in the same district. This study follows the principles of the Declaration of Helsinki. Ethical approval was provided by Biruni University Ethical Committee (CSS ref: 2019-27-43). Data collection was carried out between June 2019 and August 2019.

### Questionnaire Design

The questionnaire was developed based on previously published studies (Assali *et al.,* 2018; Cohen *et al.,* 2016; Giuliani *et al.,* 2019; Adé, Bourdon, Bussières, 2017; Pawłowska *et al.,* 2019; O'Callaghan *et al.,* 2018) and consisted of 20 short questions divided into 3 sections: socio-demographic and professional characteristics; the knowledge of pharmacists about high-tech medicines; and pharmacists' behavior and attitude towards advanced technology.

The questions of the third section consist of a 5-point Likert-type scale ranging from "Strongly disagree" to "Strongly agree". The questionnaire was reviewed for content validity by an expert in the field. Finally, based on the pre-test of 20 community pharmacists, the final version of the questionnaire was established.

### Data Analysis

Statistical analysis of the results was performed with Student's t-test and Welch Test. Student's t-test was used to test the significance of the mean difference between the two groups. In cases where the number of groups was more than 2, the Welch's t-test, one of the Robust tests, an alternative to the Anova test, was used to eliminate the homogeneity of variances problem while testing the significance of mean difference between two groups.

Tukey's test or the Bonferroni test was used when there was a difference. If the mean difference between at least 2 groups was significant in the Welch's t-test, either Tukey's test or the Bonferroni test was used to test which groups caused the difference, depending on whether the variance between groups was equal or not.

Sub-analyses were performed by pharmacists' gender, age, degree of education, years of practice, and the location of the pharmacy. The reason for analyzing the location of the pharmacy was to determine whether a relationship exists between the changing patient profile and pharmacists' perspective on technology. In all cases, the level of significance was set at $p<0.05$.

## RESULTS

The participants were randomly selected based on the frequency of pharmacies located in the districts. The socio-demographic characteristics of the participating community pharmacists are shown in Table I.

**TABLE I -** The socio-demographic characteristics of the pharmacists

| Socio-Demographics | Number (n=879) | % |
|---|---|---|
| **Age** | | |
| <26 | 44 | 5.0 |
| 26-30 | 169 | 19.2 |
| 31-40 | 295 | 33.6 |
| 41-50 | 215 | 24.5 |
| 51-60 | 86 | 9.8 |
| 60< | 70 | 8.0 |
| **Gender** | | |
| Male | 408 | 46.4 |
| Female | 471 | 53.6 |
| **Educational Level** | | |
| Bachelor (B) | 755 | 86.1 |
| Master (M) | 104 | 11.8 |
| Doctorate (D) | 18 | 2.1 |
| **Years of Practice** | | |
| 1-5 years | 192 | 21.8 |
| 6-10 years | 205 | 23.3 |
| 11-15 years | 169 | 19.2 |
| 16-20 years | 86 | 9.8 |
| 21 + years | 227 | 25.8 |
| **Location of Community Pharmacy** | | |
| Neighborhood pharmacy | 121 | 13.8 |
| Pharmacy on a street | 415 | 47.2 |
| Pharmacy near a hospital | 218 | 24.8 |
| Pharmacy near a family health center | 120 | 13.7 |
| Pharmacy in a mall | 5 | 0.6 |

In this study, the percentage of male (46.4%) and female (53.6%) participants was nearly equal. In terms of educational backgrounds, it was observed that the majority of pharmacists (86.1%) did not have master's or doctoral degrees.

**TABLE II -** Pharmacists' level of familiarity with high technology

| | Never heard n (%) | Unfamiliar n (%) | Somewhat familiar n (%) | Familiar n (%) | Very familiar n (%) |
|---|---|---|---|---|---|
| Biotechnological drugs | 25 (2.9) | 77 (8.8) | 207 (23.7) | 446 (51.1) | 118 (13.5) |
| Nanomedicines | 31 (3.6) | 73 (8.4) | 174 (20.0) | 389 (44.6) | 205 (23.5) |
| Biosimilars | 16 (1.8) | 59 (6.8) | 135 (15.5) | 403 (46.3) | 257 (29.5) |
| Generic drugs | 15 (1.7) | 39 (4.5) | 118 (13.5) | 425 (48.7) | 276 (31.6) |
| Immunogenicity | 183 (21.1) | 137 (15.8) | 215 (24.8) | 216 (24.9) | 116 (13.4) |
| 3D printing drugs | 312 (35.8) | 135 (15.5) | 184 (21.1) | 182 (20.9) | 58 (6.7) |
| Personalized medicine | 154 (17.8) | 138 (15.9) | 211 (24.3) | 269 (31.0) | 95 (11.0) |
| Recombinant DNA technology | 280 (32.3) | 182 (21.0) | 163 (18.8) | 148 (17.1) | 95 (10.9) |
| CRISPR technology | 384 (44.1) | 154 (17.7) | 150 (17.2) | 121 (13.9) | 61 (7.0) |

The percentage of very familiar and familiar responses was summed to determine the highest familiarity rate. As seen in Table II, generic drugs had the highest familiarity rate with 80.3% among the participating pharmacists. We remind you that these products are conventional drugs that are not usually manufactured with high technology. This was followed by biosimilars with 75.8%, nanomedicines with 68.1% and biotechnological drugs with 64.6%. Among the least known was CRISPR technology with 20.9% familiarity, followed by 3D printing drugs with 27.6% and Recombinant DNA technology with 28%.

According to Table III, generic drugs had the highest familiarity rate, though this differed significantly across professional experience, at least between two groups (6-10 years and more than 20 years) at a 95% confidence level.

**TABLE III -** Correlation between pharmacists' years of practice and the familiarity of generic drugs

| | | N | Mean | Std. Deviation | p |
|---|---|---|---|---|---|
| Generic drugs | 1-5 years | 191 | 3.97 | 0.888 | 0.018 |
| | 6-10 years | 202 | 3.94 | 1.040 | |
| | 11-15 years | 167 | 4.11 | 0.832 | |
| | 16-20 years | 86 | 3.94 | 0.938 | |
| | >20 years | 227 | 4.17 | 0.723 | |
| | Total | 873 | 4.04 | 0.885 | |

Although familiarity with biosimilars (75.8%) was reported to be high, only 35% of the participants responded that reference biologic products and biosimilars are not structurally identical, as shown in Table VI. Familiarity with biosimilars differed, at least between two groups, by pharmacy location at a 99% confidence level (p=0.006).

Similarly, familiarity with Immunogenicity (p=0.000, at a 99% confidence level), familiarity with 3D printing drugs (p=0.002, at a 99% confidence level), familiarity with Recombinant DNA technology (p=0.019, at a 95% confidence level) and familiarity with CRISPR technology (p=0.004, at a 99% confidence level) differed by pharmacy location (Table IV).

**TABLE IV -** Correlation between pharmacy location and the familiarity of high technology terms

| | | N | Mean | Std. Deviation | p |
|---|---|---|---|---|---|
| Biosimilars | Neighborhood pharmacy | 117 | 3.72 | 0.999 | 0.006 |
| | Pharmacy on a street | 411 | 3.94 | 0.882 | |
| | Pharmacy near a hospital | 217 | 4.15 | 0.936 | |
| | Pharmacy near a family health center | 120 | 3.83 | 1.026 | |
| | Pharmacy in a mall | 5 | 4.40 | 0.894 | |
| | Total | 870 | 3.95 | 0.941 | |
| Immunogenicity | Neighborhood pharmacy | 119 | 2.61 | 1.316 | 0.000 |
| | Pharmacy on a street | 408 | 2.79 | 1.289 | |
| | Pharmacy near a hospital | 215 | 3.28 | 1.404 | |
| | Pharmacy near a family health center | 120 | 3.16 | 1.230 | |
| | Pharmacy in a mall | 5 | 2.20 | 1.304 | |
| | Total | 867 | 2.94 | 1.336 | |
| 3D printing drugs | Neighborhood pharmacy | 118 | 2.26 | 1.336 | 0.002 |
| | Pharmacy on a street | 413 | 2.32 | 1.305 | |
| | Pharmacy near a hospital | 215 | 2.73 | 1.372 | |
| | Pharmacy near a family health center | 120 | 2.77 | 1.262 | |
| | Pharmacy in a mall | 5 | 1.60 | 1.342 | |
| | Total | 871 | 2.47 | 1.336 | |
| Recombinant DNA technology | Neighborhood pharmacy | 116 | 2.42 | 1.384 | 0.019 |
| | Pharmacy on a street | 412 | 2.41 | 1.352 | |
| | Pharmacy near a hospital | 215 | 2.81 | 1.416 | |
| | Pharmacy near a family health center | 120 | 2.63 | 1.316 | |
| | Pharmacy in a mall | 5 | 1.80 | 1.304 | |
| | Total | 868 | 2.53 | 1.376 | |

**TABLE IV -** Correlation between pharmacy location and the familiarity of high technology terms

| | | N | Mean | Std. Deviation | p |
|---|---|---|---|---|---|
| CRISPR technology | Neighborhood pharmacy | 118 | 1.91 | 1.274 | 0.004 |
| | Pharmacy on a street | 411 | 2.12 | 1.292 | |
| | Pharmacy near a hospital | 216 | 2.48 | 1.377 | |
| | Pharmacy near a family health center | 120 | 2.42 | 1.294 | |
| | Pharmacy in a mall | 5 | 1.60 | 1.342 | |
| | Total | 870 | 2.22 | 1.325 | |

Familiarity with Immunogenicity differed significantly according to the education levels of pharmacists, between bachelors B and doctorates D at a 95% confidence level (p=0.044). Similarly, familiarity with Personalized medicine (p=0.013, 95% confidence level, between B and D), Recombinant DNA technology (p=0.002, 99% confidence level, between B and M/D), CRISPR technology (p=0.014, 95% confidence level, between B and M/D) differed according to the education levels of pharmacists (Table V).

**TABLE V -** Correlation between pharmacists' education level and the familiarity of high technology terms

| | | N | Mean | Std. Deviation | p |
|---|---|---|---|---|---|
| Immunogenicity | Bachelor (B) | 744 | 2.91 | 1.319 | 0.044 |
| | Master (M) | 103 | 3.05 | 1.431 | |
| | Doctorate (D) | 18 | 3.67 | 1.283 | |
| | Total | 865 | 2.94 | 1.336 | |
| Personalized medicine | Bachelor (B) | 749 | 2.97 | 1.257 | 0.013 |
| | Master (M) | 100 | 3.22 | 1.375 | |
| | Doctorate (D) | 16 | 3.69 | 1.014 | |
| | Total | 865 | 3.02 | 1.272 | |
| Recombinant DNA technology | Bachelor (B) | 747 | 2.46 | 1.337 | 0.002 |
| | Master (M) | 103 | 3.00 | 1.534 | |
| | Doctorate (D) | 16 | 3.19 | 1.471 | |
| | Total | 866 | 2.54 | 1.377 | |
| CRISPR technology | Bachelor (B) | 751 | 2.16 | 1.274 | 0.014 |
| | Master (M) | 101 | 2.53 | 1.578 | |
| | Doctorate (D) | 16 | 3.00 | 1.506 | |
| | Total | 868 | 2.22 | 1.326 | |

The response to the statement that "biosimilars and reference biologic products are structurally identical" differed with age at a 95% confidence level (Mean_25>=2.8, Mean_26-30=2.72, Mean_31-40=2.97, Mean_41-50=2.95, Mean_51-60=2.91, Mean >60=2.65, p=0.034).

The level of agreement with this statement significantly differed according to the academic degree of the respondent at a 95% confidence level (Mean_ B=2.93, Mean_ M=2.55, Mean_ D= 2.71, p=0.012). The difference was determined between bachelors and those with master's degrees. Mostly pharmacists who had a bachelor's degree agreed with this statement. This result shows that the higher the education level, the higher the knowledge of the respondent.

As seen in Table VI, 45.9% of the respondents agreed that indications can be extrapolated from a reference biologic product to its biosimilar. The response differed by education level (Mean_ B=3.29, Mean_ M=2.92, Mean_ D=3.29, p=0.034, at a 95% confidence level), namely between masters' and bachelors'/doctorates' degrees.

Of the participants, 59% agreed that there is no difference in terms of safety, purity, and potency between biosimilars and reference biologic products. In terms of interchangeability, 31.5% of the respondents agreed that biosimilars can be safely switched with reference biologic products. Of the respondents, 20.4% agreed that biosimilars require more comprehensive data. On the other hand, it is noteworthy that the highest percentage of participants (44.7%) remained undecided. Similarly, undecided respondents constituted the highest percent for interchangeability (39.5%) and the "identical to its reference biologic product" statement (35.5%). The results confirm that pharmacists do not have a clear knowledge about biotechnological drugs.

**TABLE VI -** If the active substance (INN) of a reference biological product and a biosimilar are the same

| | Strongly disagree n (%) | Disagree n (%) | Undecided n (%) | Agree n (%) | Strongly Agree n (%) |
|---|---|---|---|---|---|
| Identical to its reference biologic product | 77 (8.8) | 229 (26.2) | 310 (35.5) | 239 (27.3) | 19 (2.2) |
| Indications can be extrapolated | 61 (7.0) | 102 (11.6) | 311 (35.5) | 365 (41.7) | 37 (4.2) |
| No meaningful differences in terms of safety | 9 (1.0) | 79 (9.1) | 269 (30.9) | 437 (50.2) | 77 (8.8) |
| They are interchangeable | 81 (9.3) | 171 (19.7) | 344 (39.5) | 222 (25.5) | 52 (6.0) |
| Biosimilars requires more comprehensive data | 75 (8.6) | 229 (26.3) | 389 (44.7) | 137 (15.7) | 41 (4.7) |

Pharmacists mostly identified the main advantage of advanced technology medicines as smart/targeted drug delivery (24.6%). Enabling targeted drug delivery was one of the prominent features of nanotechnology-based drugs. For this reason, in terms of advanced technology, the first thing that comes to community pharmacists' mind is often nanotechnology. Another remarkable result was that cost-effectiveness was rated the lowest (5.1%) among the advantages. However, cost-effectiveness is one of the greatest advantages of biosimilars. This result may be due to the perception of high technology production as an expensive process in general.

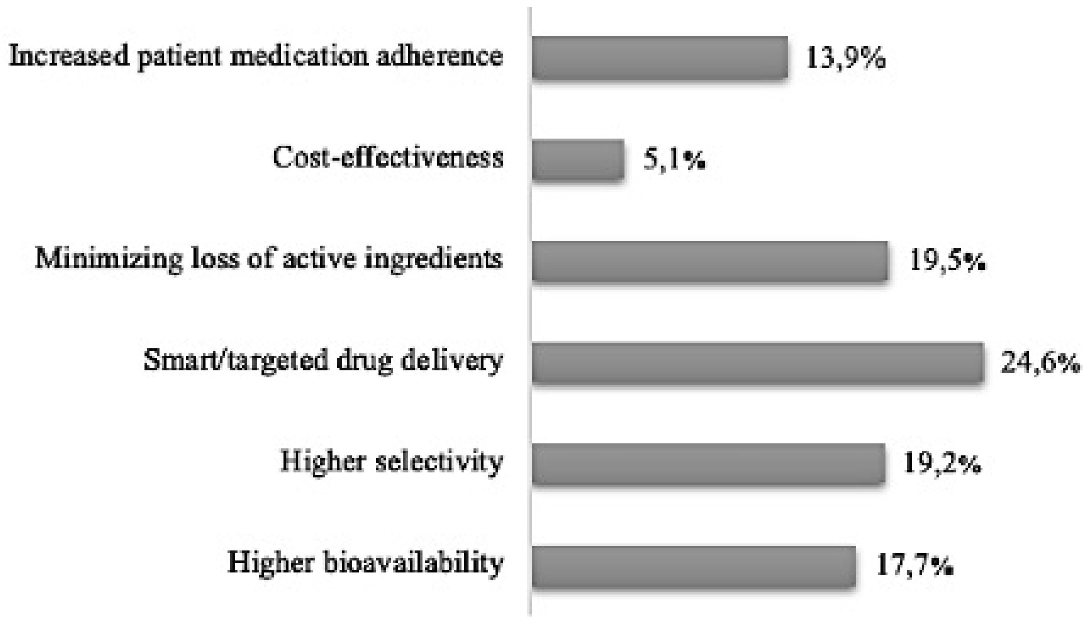


**FIGURE 1 -** The main advantages of high technology medicines.

As seen in Figure 2, among the disadvantages of 3D-printed drugs, which enjoy a relatively low level of familiarity (27.6%), the length of processing time was rated highest (22%). The closest answer was "no idea", with a rate of 21.4%. It is noteworthy that "limitations in the commercialization" was rated lowest with 7.5%. However, stability problems and the inability to process many thermosensitive active ingredients emerge as challenges that must be overcome in 3D printing of drugs.

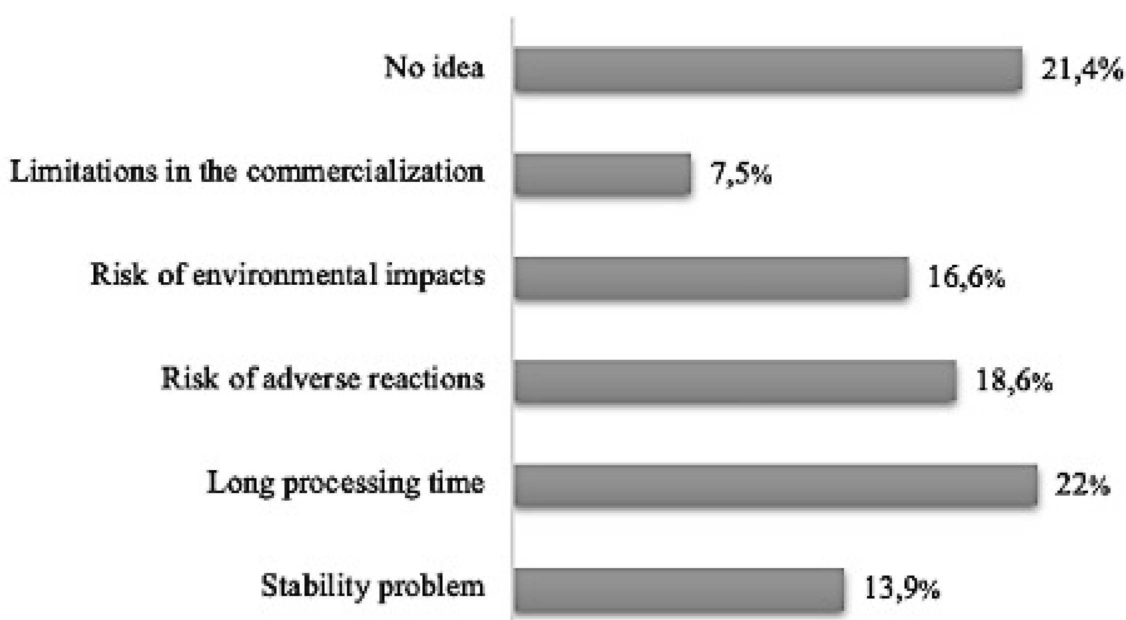


**FIGURE 2 -** The most important challenges to overcome in 3D-printing of drugs.

Due to the harm that advanced technology medicines may cause to the patient, the ethical code of "Primum non nocere", namely "first, do no harm", which is included in the Hippocratic oath, stands out as one of the most important ethical problems (31.7%). This ethical principle is also among the primary ethical codes of pharmacy practices. Pharmacists highlighted providing benefits at a rate of 30.0%.

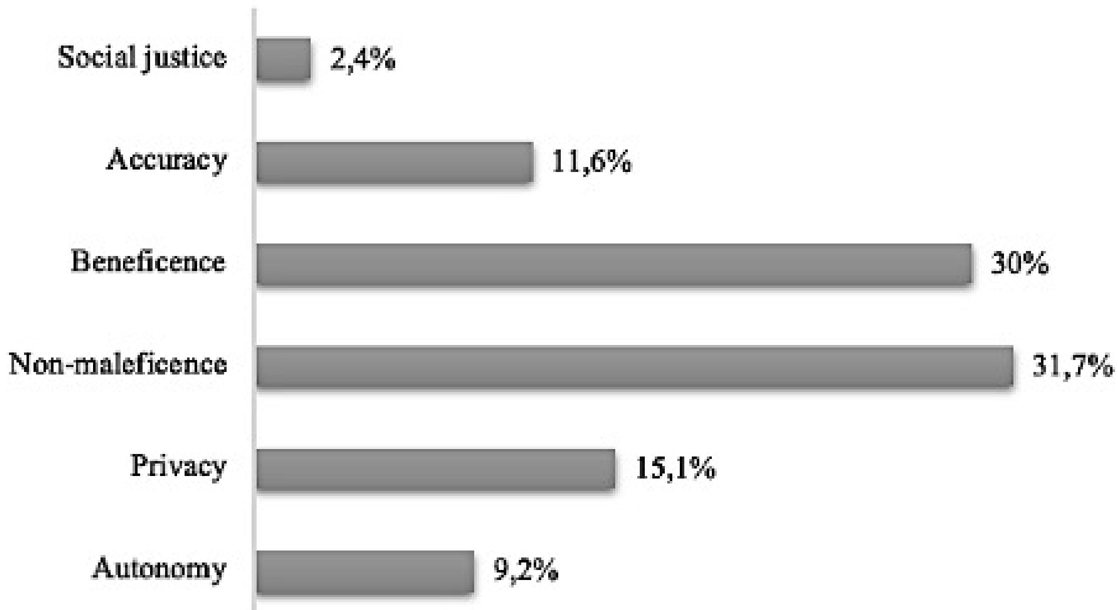


**FIGURE 3 -** The most important ethical code with advanced technology drugs.

Although social justice had the lowest rate (2.4%) among ethical problems, nano-divide increases the inequality gap between rich and poor countries. Likewise, the high cost of reference biotechnology products appears to be a serious ethical problem preventing the access of many patients. Biosimilars may serve as cheaper alternatives at this point.

The rate of agreement with statements related to high technology drugs was measured using a Likert scale and the results are listed in Table VII.

**TABLE VII -** Frequency distribution of pharmacists according to 5-point Likert scale

| | Strongly disagree n (%) | Disagree n (%) | Undecided n (%) | Agree n (%) | Strongly Agree n (%) |
|---|---|---|---|---|---|
| I support the development of advanced technology medicines | 24 (2.7) | 95 (10.9) | 312 (35.7) | 332 (37.9) | 112 (12.8) |
| During reporting an adverse reaction on biotechnology-based medicines, the batch number and the brand name are required | 4 (0.5) | 32 (3.7) | 177 (20.2) | 499 (57) | 163 (18.6) |
| I am concerned about the genetic interventions applied to living things | 33 (3.8) | 78 (8.9) | 183 (21.0) | 351 (40.2) | 228 (26.1) |

**TABLE VII -** Frequency distribution of pharmacists according to 5-point Likert scale

| | Strongly disagree n (%) | Disagree n (%) | Undecided n (%) | Agree n (%) | Strongly Agree n (%) |
|---|---|---|---|---|---|
| I support genome editing technology for the future of humanity | 8 (0.9) | 55 (6.3) | 211 (24.1) | 482 (55.1) | 118 (13.5) |
| Nanotechnology-based drugs are completely safe | 16 (1.8) | 112 (12.8) | 387 (44.4) | 316 (36.2) | 41 (4.7) |
| Every segment of society equally benefits from nanotechnology | 34 (3.9) | 103 (11.9) | 317 (36.6) | 347 (40.0) | 66 (7.6) |
| 3D printing technology is not suitable for pharmaceutical manufacturing | 22 (2.5) | 96 (11.0) | 384 (44.1) | 301 (34.6) | 67 (7.7) |
| 3D printing technology can be used in pharmacy practice | 10 (1.1) | 71 (8.1) | 308 (35.0) | 385 (44.1) | 99 (11.3) |
| There is a safety risk in advanced technology medicines in general | 11 (1.3) | 79 (9.0) | 357 (40.8) | 347 (39.7) | 80 (9.2) |
| I want to receive more detailed training on the use of advanced technology medicines | 11 (1.3) | 69 (7.8) | 281 (32.0) | 407 (46.6) | 105 (12.0) |

The rate of accord with the statement “I support the development of advanced technology medicines” was 50.7%. Although the percentage of pharmacists who disagreed with this statement was 13.6%, the percentage of those who remained undecided stands out at 35.7%.

The rate of agreement with the statement “During reporting an adverse reaction on biotechnology-based medicines, the batch number and the brand name are required” was 75.6%. This expression was found to differ by gender at a 95% confidence level (Mean_ Male=3.84, Mean_Female=3.95, p=0.029)

Almost two-thirds of participants (66.3%) agreed with the statement “I am concerned about the genetic interventions applied to living things”. In contrast, the percentage of those who are not worried was 12.7%. This expression also differed by gender at a 95% confidence level (Mean_ Male=3.68, Mean_Female=3.83, p=0.035). It was found that women were more worried about both of these statements than men.

The rate of agreement with the statement “I support genome editing technology for the future of humanity” was 68.6%. The rate of those who did not support it was quite low (7.2%). The response to this statement was found to differ significantly by level of education (Mean_ B=3.72, Mean_ M=3.82, Mean_ D=4.17, p=0.031, at a 95% confidence level). It was seen that those with doctorate degrees mostly accepted and supported genome editing technology. While 40.9% of the pharmacists agreed that “Nanotechnology-based drugs are completely safe”, the responses differed by age at a 90% confidence level (Mean_25>=3.25, Mean_26-30=3.12, Mean_31-40=3.32, Mean_41-50=3,35, Mean_51-60=3.39, Mean>60=3.32, p=0.092). The difference was between the 26-30 and 51-60 age ranges. At the same time, the responses differed by professional experience at a 99% confidence level (Mean_1-5years=3.02, Mean_6-10years=3.43, Mean_11-15years=3.29, Mean_16-20years=3.39, Mean_>20 years=3.36, p=0.000). Accordingly, pharmacists with the least professional experience – 1-5 years – were differed significantly from all the other groups. Differences were also determined by pharmacy location, namely between “neighborhood pharmacy” and “pharmacy in a mall” (Mean_ Neighborhood pharmacy=3.17, Mean_ Pharmacy on a street=3.28, Mean_ Pharmacy near a hospital=3.38, Mean_ Pharmacy near a family health center=3.29, Mean_ Pharmacy in a mall=3.80, p=0.052, at a 90% confidence level).

Similarly, there was a difference according to education level (Mean_ B=3.31, Mean_ M=3.10, Mean_ D=3.78, p=0.009, at a 99% confidence level). The difference was determined between bachelors/masters and those with doctorate's degrees. It was seen that those with doctorate degrees agreed more with this statement.

Of the pharmacists, 47.6% agreed with the statement "Every segment of the society equally benefits from nanotechnology". However, nano-divide appears to be the primary ethical problem. The approach to this problem differed by the pharmacy location. (Mean_ Neighborhood pharmacy=3.09, Mean_ Pharmacy on a street=3.33, Mean_ Pharmacy near a hospital=3.52, Mean_ Pharmacy near a family health center=3.45, Mean_ Pharmacy in a mall=2.8, p=0.004, at a 99% confidence level).

Similarly, the rate of agreement with this statement differed bye level of education between bachelors and master's/doctorate degree (Mean_ B=3.38, Mean_ M=3.13, Mean_ D=3.53, p=0.048, at a 95% confidence level).

The rate of agreement with the statement "3D printing technology is not suitable for pharmaceutical manufacturing" was 42.3%, the response to which differed by level of education (Mean_ B=3.38, Mean_ M=3.04, Mean_ D=3.61, p=0.003, at a 99% confidence level). Pharmacists with master's degrees showed less agreement with this statement than others.

Of the pharmacists, 55.4% agreed that "3D printing technology can be used in pharmacy practice". Similar to confidence in nanotechnology-based medicines, opinion on using 3D printing technology in pharmacy practice differed by age at a 90% confidence level. It was observed that 48.9% of the participants agreed that "There is a safety risk in advanced technology medicines in general". The percentage of those who wanted to receive training in advanced technology medicines was determined to be 58.6%. The response differed by education level (Mean_ B=3.57, Mean_ M=3.75, Mean_ D=4.00, p=0.032, at a 95% confidence level). It was observed that pharmacists with doctorate degrees were more willing to receive additional training.

## DISCUSSION

Lack of knowledge and the need for education among pharmacists, which is one of the most prominent results of our study, has also been emphasized in previous studies (Assali *et al.,* 2018; Cohen *et al.,* 2016; Giuliani *et al.,* 2019; Leonard *et al.,* 2019; Adé, Bourdon, Bussières, 2017; Pawłowska *et al.,* 2019; O'Callaghan *et al.,* 2018).

Pharmacists should be well-informed about advanced technology medicines. Taking the current COVID-19 pandemic into account, creating online-based interactive training modules will increase the participation of pharmacists. As pharmacists gain more knowledge, the mist of uncertainty will dissolve, and confidence will be established.

In a study conducted by O'Callaghan *et al.* (2018), they found that Irish community pharmacists were familiar with the term of biosimilars (77%) – data which corresponded almost exactly to our results (75.8%). The same study also determined that 47% of all healthcare professional participants agreed that two biological medicines with the same INN would have an identical structure, whereas our findings showed that only 29.5% community pharmacists mistakenly agreed with this statement. The fact that the two studies were conducted in different time periods may explain this divergence in the findings. It is known that biosimilars are not generics because they are similar but not identical, unlike conventional drugs. It was seen that 65% of the pharmacists participating in our study, including the undecided participants, lacked this basic knowledge about biosimilars (Table IV).

According to our study results, it was found that familiarity with high technology drugs varies according to the location of the pharmacy (Table IV). The reason may be that patients' medication profiles and interest in advanced technology vary depending on the pharmacy's location. At the same time, familiarity with technologies less known among pharmacists, such as CRISPR technology and Recombinant DNA Technology, have been shown to differ significantly according to the education levels of pharmacists (Table V). It has been observed that the higher the education level, the higher the familiarity of the respondent. This result has been confirmed in terms of the knowledge of the respondent regarding biotechnological products. A relatively high rate of undecided participants is also noteworthy, highlighting the knowledge gaps that exist among pharmacists (Table VI).

We may assume that pharmacists have a perception that high technology is expensive because cost-effectiveness is rated lowest among the main advantages (5.1%) (Figure 1). The fact that the most important ethical issue regarding high technology products is non-maleficence (31.7%) shows that pharmacists are aware of the possible risks related to these products and that they have mastered the basic ethical codes of pharmacy practice (Figure 3).

The concerns of community pharmacists about advanced technology medicines are included in our research results. Female pharmacists were found to be particularly concerned (Table VII). However, the reasons for anxiety are not within the scope of this study and require further studies. At the same time, our study determined that 68.6% of pharmacists supported genome editing technology. All these results show that pharmacists seem to support gene technology studies, while feeling at the same time that it raises ethical questions, as evidenced by a lack of confidence revealed in these studies. At this point, it is important to provide evidence-based education (Cohen *et al.,* 2016). According to Table VII, 48.9% of the participants agreed that “There is a safety risk in advanced technology medicines in general”. For this reason, assigning the necessary importance to balancing the benefits and risks to public health and the environment in advanced technology drugs will increase the confidence of pharmacists in such medicines. Without ignoring the possible safety risks of these products, it should be ensured that the pharmacist adopts these products with a broader awareness.

It is important to properly establish communication strategies that transfer information in order to eliminate these concerns. In this context, it is necessary to establish a communication bridge between healthcare professionals and scientific research, to create the building blocks of this bridge from clear and transparent information that covers the possible risks and benefits of advanced technology medicines, and to build trust. Thus, the scientific literacy of pharmacists, physicians, and other healthcare professionals can be increased, and they can guide society as a thought leader towards technological advancements in healthcare.

## CONCLUSION

Pharmacists and other healthcare professionals are required to adapt to the pace of developments in advanced technology medicines. High-tech medicines will be more common in pharmacies in the future. For this reason, pharmacists are required to update their knowledge about advanced technology medicines and take responsibility to guide society. Extended data obtained by performing similar studies in other countries will enable both healthcare professionals and patients to derive greater benefit from technological innovations..

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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