Prospectus

Optimization of the Production of Lofexidine
(Technical Topic)

Instagram's Effect on self-objectification and body image issues among young women
(STS Topic)

By

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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Introduction

According to the National Institute on Drug Abuse, approximately 2.1 million people in the United States abuse opioids. Opioid addiction has become an increasing epidemic in the United States with the death rate rising significantly. The number of opioid deaths is projected to increase from 33,100 in 2015 to 81,700 by 2025, a 147% increase (Chen et al., 2019). In October of 2017, the United States Department of Health and Human Services declared the opioid crisis a national public health emergency. Currently, popular medications prescribed to treat opioid addiction are actually opioids. The technical aspect of this prospectus focuses on the scaleup production of Lofexidine, a non-opioid medication that helps patients withdraw, and it was approved for use in the United States in 2018. Lofexidine contains a central alpha 2-adrenergic agonist, which decreases the release of norepinephrine. This reduces the neurochemical surge that produces withdrawal symptoms in opioid abusers. Since Lofexidine costs significantly more than other opioid withdrawal medications, uptake in the United States has not been significant. The technical project will analyze the production of Lofexidine in an industrial scale to gain insight in optimal operating conditions which result in cheaper manufacturing costs and lower Lofexidine pricing.

Technical Topic

The United States Department of Health and Human Services declared the opioid crisis a national public health emergency in October 2017. According to the National Institute of Drug Abuse, more than 130 people in the United States die every day after overdosing on opioids. United States overdose deaths involving opioids rose from 8,148 in 1999 to 47,000 in 2017 (National Institute of Drug Abuse, 2019). Opioids include prescription pain relievers, heroin and other synthetic narcotics such as fentanyl. Addiction often persists for years before

serious health problems become apparent; increases in the rate of hospital visits due to opioid misuse and inquiries into addiction treatments consistently rise faster than morbidity (Kolodny et al., 2015). Adverse symptoms resulting from discontinued usage (withdrawal) are a significant driver of addiction. Understanding the economic burden of adverse health outcomes is essential when considering cost-effective prevention strategies. The U.S. economic burden -- including healthcare and substance abuse treatment cost, criminal justice and cost productivity -- was estimated to be over $78.5 billion in 2013 (Florence et al., 2013). This technical project focuses on optimizing the scaleup production of Lofexidine, an opioid withdrawal medication, to result in cheaper manufacturing and drive Lofexidine prices down.

Before Lofexidine, a majority of the recommended medications for management of opiate withdrawal were other opioids, with methadone and buprenorphine-naloxone being the most common. The propensity of patients, or people struggling with opiate addiction, to become addicted to these medications necessitated a non-addictive product for withdrawal management. Lofexidine is a non-opioid, alpha-2-adrenergic agonist prescription medication that works to block the release of norepinephrine, a hormone with similar chemical properties to that of adrenaline, which is responsible for many of the experienced withdrawal symptoms. Lofexidine proves to be slightly safer than clonidine, its largest competitor, as clonidine has been found to cause hypotension, a side effect not found with Lofexidine. Similarly, through clinical studies, it has been shown that the withdrawal symptoms are resolved sooner with Lofexidine compared to tapered dosing of methadone, resulting in a shorter treatment period (Wakeman, 2018). Data collected on 1,074 opiate detoxifications conducted with Lofexidine in the United Kingdom showed successful results in more than 60% of the subjects at a mean of 10 days of

detoxification (Akhurst, 1999), further demonstrating the effectiveness of Lofexidine in a short timescale.

Lofexidine was first sold in the United Kingdom to treat opiate withdrawal symptoms under the name Britlofex in 1992. However, doubts concerning the drug's effectiveness and value compared to a similar compound, clonidine, delayed the United States from considering the medicine until a more substantive clinical study was submitted in 2016 (Rehman et al., 2019). United States approval quickly followed in 2018, allowing it to be marketed under the name Lucemyra. However, the drug has not garnered much attention in the USA because generic clonidine is still cheaper by a factor of 20 and marketing has generally failed to entice investors (Solorio, 2018).

The technical project will analyze all details necessary for the effective scaleup of a five-step process detailed in 2008 for synthesis and isolation of Lofexidine from enantiopure methyl lactate and 2,6-dichlorophenol, outlined in *Figure 1* (Crooks & Vartak, 2012). As an overview, the starting material, an enantiomer of methyl lactate, is reacted with 2,6-dichlorophenol, triphenylphosphosphine, and diisopropyl azodicarboxylate to create 1-methyl-1-[2,6-dichlorophenoxy]ethanoate. Next, the 1-methyl-1-[2,6-dichlorophenoxy]ethanoate is converted to 1-methyl-1-[2,6-dichlo rophenoxy]ethanamide through treatment with ammonia. The third step of the synthesis involves the conversion of 1-methyl-1-[2,6-dichlo rophenoxy]ethanamide to an imino-ether intermediate through an electrophilic attack by a trimethoxonium ion to the amide oxygen, and further converting the intermediate to 2-[1-(2,6-dichlo rophenoxy)-ethyl]1,3-diazacyclopent-2-ene by adding ethylene diamine. Finally, the resulting product can be converted into a pharmaceutically functional acid salt through treatment with aqueous hydrochloric acid.

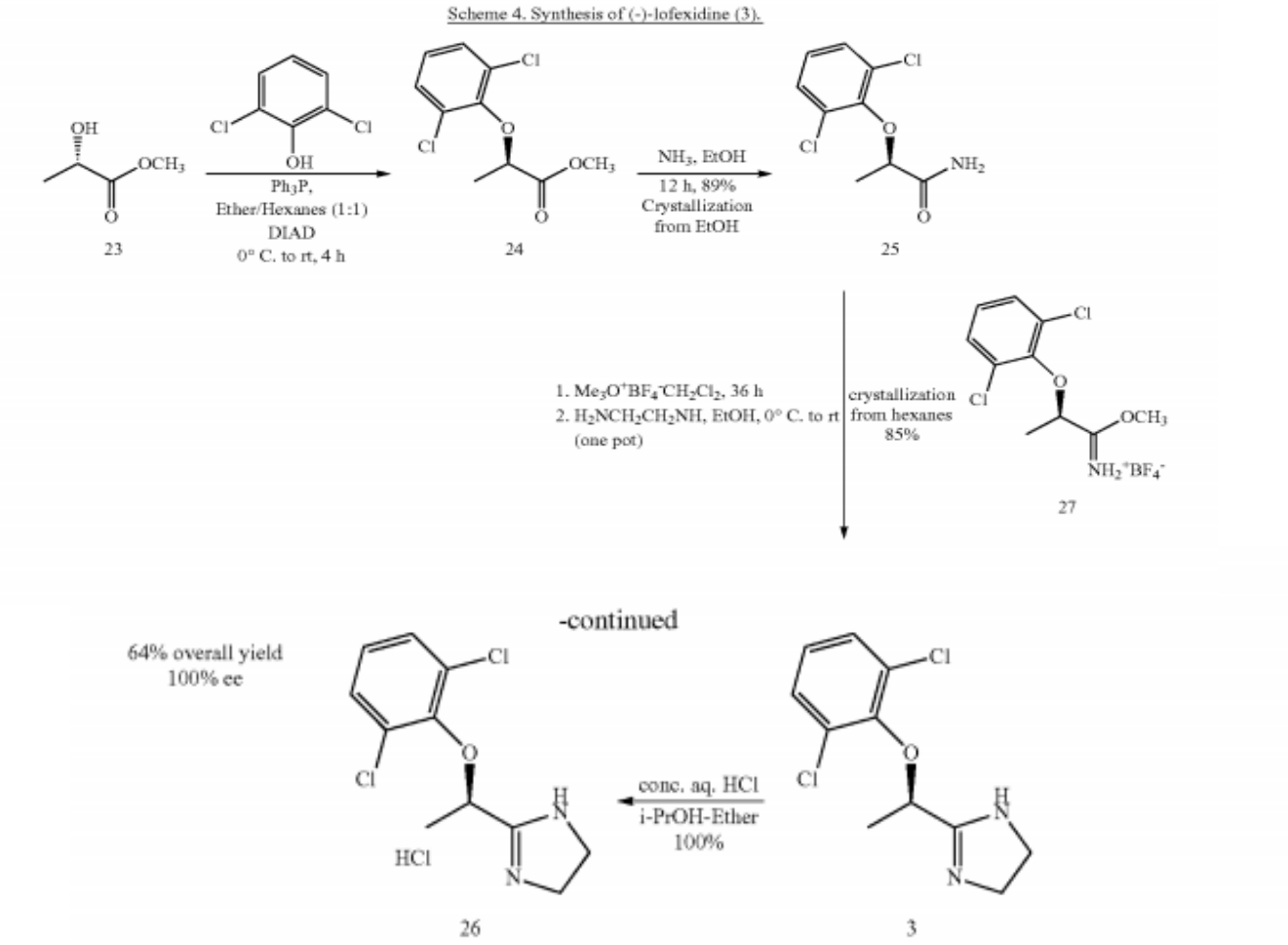

Figure 1: Proposed Five-Step Synthesis Process of Lofexidine for Scale-Up (Crooks & Vartak, 2012)

If the other stereoisomer of Lofexidine is desired, the alternate enantiomer of methyl lactate must be used in the first reaction of the synthesis. The two enantiomeric forms show significant differences in their α_2-adrenergic receptor affinities, which affect the molecule's capacity to lower mean arterial blood pressure. As illustrated in Figure 1, the process incorporates three low temperature reactions and two crystallizations, necessitating the design of five apparatuses to produce the compound at high rates. However, the proposed synthesis is more

efficient than other proposed mechanisms, as it does not require additional purification techniques such as distillation or column chromatography and returns the desired product in a yield of roughly 64%, which is roughly triple that of the next best proposed synthesis (Crooks & Vartak, 2012). Due to resource limitations, testing of equipment designs and specifications will be executed in Aspen Plus Version 11. Economic analysis will incorporate equipment installation costs from manufacturing memorandums, operational power requirements estimated by the Aspen software, waste management costs from environmental agencies or manufacturing memorandums if processed on site, and a competitive price for the drug based on the Chinese sale price, which totals roughly $1,776 for 84 tablets lasting the initial seven-day treatment period (Bryce, 2019). A design basis memorandum will be formulated in December to address production, safety concerns and maintenance protocols. Economic analysis will follow in February with a full process demonstration in March to precede the completed technical report.

STS Topic

While the opioid crisis driving the technical project has significant human and social dimensions, the societal aspect of this prospectus transitions to examining the effect Instagram, a popular social media platform, has on self-objectification and body image issues in young women. Instagram is a photo-based software application that allows users to take, edit and share photographs with their followers. Founded by two men, Kevin Systrom and Mike Kriegerm, Instagram became available on the iPhone app store in 2010. As of June 2018, Instagram reached one billion active users, with more than 500 million daily users. The focus of this prospectus is on the young adult age group since 71% of Instagram users are under the age of 35 (Moshin, 2019). Women, in particular, are more susceptible to the negative effects of self-objectification and experience a higher likelihood of mental health consequences associated with

body dissatisfaction than men (Vuković et al., 2018). Other social media platforms, such as Facebook, Snapchat, and Twitter, may have similar effects but this prospectus focuses on Instagram with its growing popularity and heavily photo-based content. Considering Instagram's primary use is posting and sharing images, researchers have suggested that Instagram may be more detrimental to women's appearance concerns than other social media platforms that contain more varied content (Fardouly et al., 2018). With Instagram being so prevalent in this generation, this prospectus investigates the negative effects this new technology has on the well-being of young women.

Instagram allows users to upload, edit with an abundance of filters, and share photos and videos with followers. Other features of Instagram include direct messaging and "stories" that stay on the user's profile for 24 hours. A user's home feed consists of posts from those they follow, and users can "like" and comment on other users' posts. Previous research suggests media may lead to greater body dissatisfaction in women through two pathways – the tendency to compare appearance to others and internalization of societal beauty ideals (Van den Berg et al., 2002). Images posted on Instagram are often carefully selected, edited and enhanced, which portrays a heightened society beauty ideal. Facebook bought Instagram in April of 2012 in a one-billion-dollar acquisition when Instagram had only six engineers. Now Instagram, a company estimated to be worth over $100 million (if it were a stand-alone company) constructing a product with over 1 billion users, only has about 100 engineers (McCormick, 2018., McCracken, 2015). This project investigates how the "programming" of these 100 engineers has affected the lives of young women users with regards to self-objectification and body image issues.

Discussing the technical dimensions of Instagram is crucial to understanding how this technology is gaining popularity. In a study of 613 participants, respondents were asked to rate the gratifications and technical attributes of Instagram and Facebook that have led to increase time spent each app. Respondents indicated the openness, defined as extent to which personal contents are open to other users, and browsing aspect of Instagram has led to an uptake in use over Facebook (Kim & Kim, 2019). At launch, Instagram utilized a chronologically based algorithm to develop the user's feed which placed the users' followers' post in a chronological order. In July of 2016, Instagram launched a relevancy-based algorithm which relies on machine learning based on past behavior to create a unique feed for every user determined on three factors – interest, recency and relationship. This new algorithm may be increasing the detrimental effects of Instagram due to machine learning prioritizing these harmful posts.

The objectification theory argues how women are accultured to internalize an observer's perspective on their physical self (Fredrickson & Roberts, 1997). Self-objectification and accompany body-surveillance can negatively affect the quality of life in young women through withdrawing from life-sustaining activities due to low self-esteem, self-harm and decreased sexual enjoyment (Brajdić et al., 2018). Saunders and Eaton (2018) studied what social-networking platforms – Facebook, Instagram, and Snapchat – were most related to body dissatisfaction in young women. From their 637 women respondents with a mean age of 21.3, they concluded the strongest relationship between body dissatisfaction and excessive use were found on Instagram and Facebook. Interestingly, participants were more likely to use Instagram and Snapchat for passive social-networking purposes, which is linked to decrements in a user's well-being by social comparison (Saunders & Eaton, 2018). Feltman and Szymanski (2017) conducted an online survey with 492 college-aged women respondents to examine the

relationship between both self-objectification and body surveillance and Instagram, specifically. They concluded upward comparison, which is comparing yourself to someone you perceive as "better" than you, through Instagram links to self-objectification and body surveillance, but downward comparison does not (Feltman & Szymanski, 2017). Downward comparison is comparing yourself to someone you perceive as "lower" than you. One recent Instagram phenomenon is the rise of Instagram influencers, which are typically people who align with society's beauty ideal, selling products for a company. These influencers may lead to more upward comparison. The different user groups, such as influencers and non-influencers, using Instagram for different purposes leads to the societal framework of Social Construction of Technology (SCOT).

SCOT relates to how Instagram has been adapted and used by different social groups. Pinch and Bijker (2008) define SCOT as the variation and selection of the development process of a technological artifact. They discuss how the different social groups and the meanings these social groups give the artifact all must be considered in the societal development of the article. Using a bicycle as an example, they argue considering some social groups, like "anti-cyclists," may be less obvious but necessary and power and economic strength must be considered, when relevant (Pinch & Bijker, 2008). A variety of different social groups, such as young users, celebrities, influences, companies, and nonusers, must be considered when examining the influence of Instagram. In a later journal, Bijker argues the importance of constructing a world for the next generations that can handle upcoming challenges by investing in societal institutions and how the sociology of technology must evolve as new technology is introduced (Bijker, 2017). It is important to study the physiological issues caused by the relatively new technology of Instagram to better equip future generations.

Research question and methods

This study examines how the rise of Instagram in today's society has caused an increase in self-objectification and body image issues in young women. More specifically, this study will focus on Instagram's relationship with body surveillance in regard to what components of appearance are dominant in the comparison process. Previous research has been conducted on this topic with respect to Facebook, but not Instagram. A study, consisting of 112 women between the ages of 17 and 25, used visual analog scales in a survey where participants would rate their mood on a scale from 0 to 100, in regard to different appearance components, after being exposed to Facebook. Results found an increase in Facebook usage led to a significant desire in the young women to change their face, hair, and skin-related features (Fardouly et al., 2015). Surprisingly, Facebook exposure did not have an overwhelming effect on the desire for them to change their body. Two possible predictions for this result were presented: the wide range of body types and the abundance of self-portraits on Facebook (Fardouly et al. 2015). With the plethora of fitness Instagram accounts, showing off idealistic body types, this study will investigate how Instagram differs from Facebook in what appearance traits are most susceptible to body surveillance.

A similar survey with visual analogous scales will serve as the primary source of evidence collection in this study. The survey will ask participants to rate their mood with respect to different traits both prior to and after Instagram exposure. Average scores from before and after Instagram exposure will be compared to examine Instagram's effect. The participants will be asked to provide their demographics so farther study can investigate how different demographic groups are affected differently from Instagram, relating to SCOT. This method

was chosen based on the reliable results and conclusions that were able to be drawn from the study focusing solely on Facebook.

Timeline and expected outcomes

The technical project will conclude with a design on an industrial scalable manufacturing process for Lofexidine. This design deliverable will deliver insight on how to drive Lofexidine manufacturing costs down. As a result, the Lofexidine price could decrease and a safer opioid withdrawal medication may have uptake in the market.

The outcome of the science, technology and society project will provide data and analysis on how Instagram effects young women with respect to self-objectification and body image issues. In January, the survey with the visual analogous scales will be constructed, and the target sample populated will be outlined. In February, the survey will be sent out and additional research will be conducted to build a stronger case. Results of the survey will be analyzed in March and presented in the final prospectus in April. The final deliverable will bring an understanding on the self-objectification issues associated with Instagram and what specific appearance traits are most susceptible to body surveillance. These results will provide suggestions on what Instagram positivity campaigns should target.

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