Pharmacokinetic and Pharmacodynamic Evaluation of JL ENDS, Comparator ENDS, Combustible Cigarette, and Nicotine Gum Among Adult Smokers

Nicholas I. Goldenson, PhD; Joshua G. Vose MD, MBA; Mark L. Rubinstein, M.D., Joanna Jay, BA; Erik M. Augustson, PhD, MPH. JUUL Labs, Inc., San Francisco, CA, USA

Introduction

• Recent evidence indicates that the nicotine delivery of the JL electronic nicotine delivery system (ENDS; JUUL Labs, Inc.), an ENDS that utilizes a nicotine salt formulation, approximates the nicotine delivery of combustible cigarettes.[1-3]

• This confinement evaluated the nicotine delivery and subjective effects of JL ENDS compared to usual brand (UB) combustible cigarettes, nicotine gum and a comparator ENDS.

Methods

• JL ENDS-naïve adult smokers (N=65; 50.8% female; mean age=41.2) completed a 7-arm within-subjects cross-over product administration study while confined to a clinical laboratory setting for seven days.

• On each study day, participants were instructed to take 10 three-second puffs, 30 seconds apart, of each test product except for nicotine gum ("chew and park"):

1. JL ENDS - Virginia Tobacco (5% nicotine)
2. JL ENDS - Mint (5% nicotine)
3. JL ENDS - Creme (5% nicotine)
4. JL ENDS - Mango (5% nicotine)
5. UB cigarette
6. Comparator ENDS (VUSE Solo; 4.8% nicotine)
7. Nicotine gum (4 mg)

• After each product administration, nicotine delivery pharmacokinetics and ratings of product appeal and subjective effects including "product liking" (visual analog scale [VAS] 0-100), "intent-to-use-again" (VAS 0-100) and a composite "Satisfaction" subscale (modified Product Evaluation Scale [mPES]) were assessed.

• Differences between test product conditions were assessed with multi-level linear models.

Results

• Nicotine delivery of the UB cigarette was significantly higher than that of all JL ENDS product conditions, the comparator ENDS, and nicotine gum as assessed by maximum plasma nicotine levels ($C_{max\text{-}BL}$), rate of plasma nicotine rise and overall nicotine exposure ($AUC_{0\text{-}30\text{-}BL}$) (**Figures 1-3**).

• All of the JL ENDS conditions produced significantly higher $C_{max\text{-}BL}$, rate of plasma nicotine rise and $AUC_{0\text{-}30\text{-}BL}$ than nicotine gum, except $C_{max\text{-}BL}$ of Creme did not significantly differ from nicotine gum (**Figures 1-3**).

• Mean time to maximal plasma nicotine concentration (T_{max}; minutes) was significantly shorter in the JL ENDS conditions compared to nicotine gum ($p<0.001$), and T_{max} for JL ENDS did not significantly differ from the UB cigarette or comparator ENDS (**Figure 3**).

• Product liking and intent-to-use-again for the UB cigarette were rated significantly higher than each of the four JL ENDS flavor conditions, the comparator ENDS and nicotine gum (**Figure 4**).

• The Mint, Mango and Creme JL ENDS products were rated significantly more appealing than the nicotine gum and comparator ENDS (**Figure 4**).

• For the "Satisfaction" subscale of the mPES, the JL ENDS mean scores were significantly lower compared to the UB cigarette, and significantly greater than nicotine gum and comparator ENDS except Virginia Tobacco (**Figure 4**).

• Within the JL ENDS product flavor conditions, the Mint and Mango products' mean scores were significantly higher compared to Virginia Tobacco and Creme on measures of product appeal (**Figure 4**).

Figure 1. Plasma Nicotine Concentration Profiles of Combined JL ENDS products, UB Cigarette, Comparator ENDS and Nicotine Gum 120-Minutes Post-Controlled Product

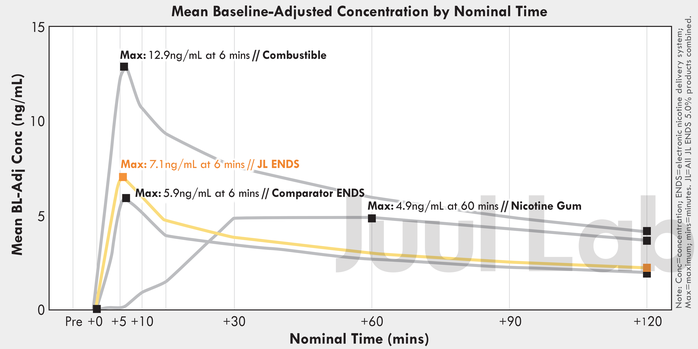


Figure 2. Plasma Nicotine Concentration Profiles of JL ENDS products 120-Minutes Post-Controlled Product Administration

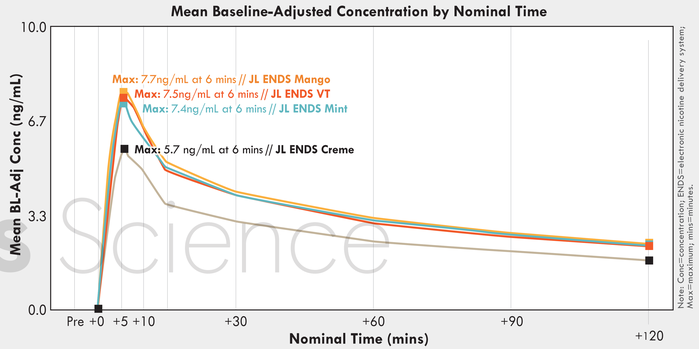


Figure 3. Plasma Nicotine Area under the Curve, $C_{max\text{-}BL}$ and T_{max} of JL ENDS, Combustible Cigarette, Comparator ENDS and Nicotine Gum (M±*SE*)

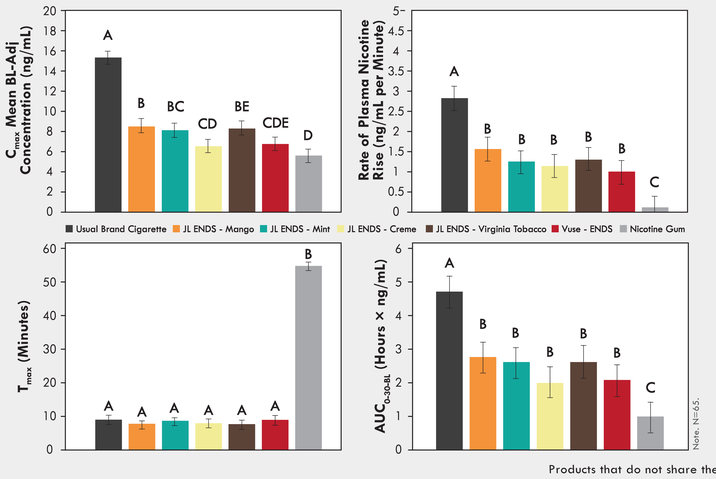
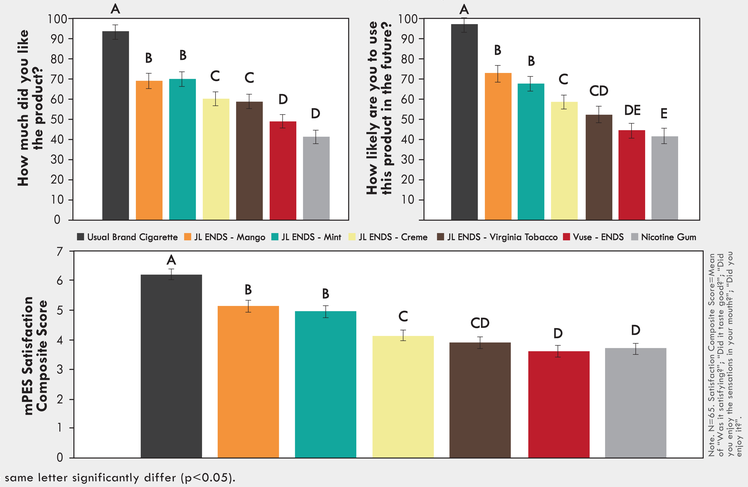


Figure 4. Product Appeal of JL ENDS , Combustible Cigarette, Comparator ENDS and Nicotine Gum (M±*SE*)



Products that do not share the same letter significantly differ ($p<0.05$).

Conclusions

• Controlled administration of JL ENDS among adult smokers resulted in nicotine delivery and product appeal that were less than that of the UB combustible cigarette but greater than nicotine gum.

• Overall, the pharmacokinetic and pharmacodynamic profiles of the JL ENDS product suggest that its abuse liability is substantially lower than the UB cigarette and higher than 4 mg nicotine gum.

• JL ENDS may have sufficient nicotine delivery and product appeal to support substitution for combustible cigarettes among adult smokers.

References

1. Yingst JM, Hrabovsky S, Hobkirk A, Trushin N, Richie JP, Jr., Foulds J. Nicotine Absorption Profile Among Regular Users of a Pod-Based Electronic Nicotine Delivery System. *JAMA Netw Open*. 2019;2(11):e1915494.

2. Hajek P, Pittaccio K, Pesola F, Myers Smith K, Phillips-Waller A, Przulj D. Nicotine delivery and users' reactions to Juul compared with cigarettes and other e-cigarette products. *Addiction*. 2020. doi: 10.1111/add.14936.

3. Maloney S, Eversole A, Crabtree M, Soule E, Eissenberg T, Breland A. Acute effects of JUUL and IQOS in cigarette smokers. *Tob Control*. 2020.