



Science ◀ Health ◀
Food ◀ Innovation

Food design in clinical trials: the impact of food formulation on absorption and metabolism of bioactive compounds

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Institute of
Food Science
+ Technology **ifst**

OSU Food Science Department



OSU Medical Center



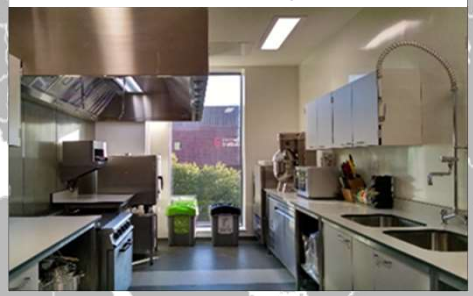
OSU Agriculture Campus- Wooster



Quadram Experimental Kitchen

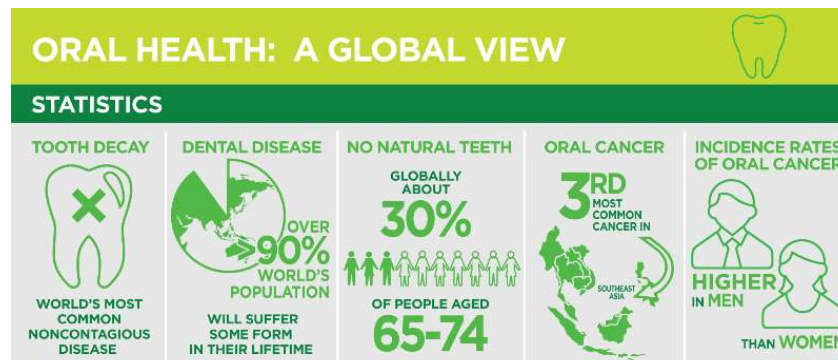


Clinical Research Facility Test Kitchen

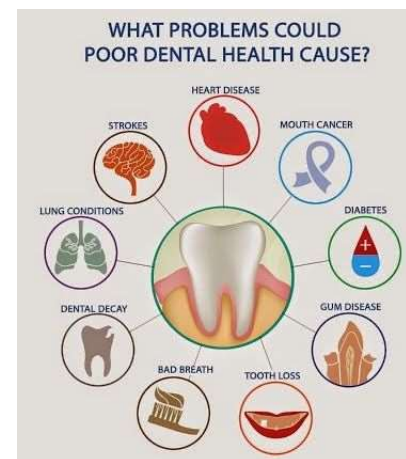


Importance of Oral Disease

- Global Burden of Disease 2015 study reports that an estimated 3.5 billion people are affected with oral disease¹.
- Untreated caries is the most prevalent oral condition in the world.
- Oral disease is linked to many diseases^{2,3}



Source: Facts are from the International Dental Federation and the World Health Organization. All Cigna products and services are provided exclusively by or through operating subsidiaries of Cigna Corporation. The Cigna name, logo and other Cigna marks are owned by Cigna Intellectual Property, Inc.



<https://doctorbrianwest.com/services/mouth-body-connection/>

¹Kassebaum, N.J. et al *J Dent Res* 2017;96:380-387

²Williams, R.C. et al *Curr Med Res Opin* 2008;24:1635-43

³Kaye, E.A. *J Am Dent Assoc* 2007;138:616-9.

Oral Health and Diet

- Diets rich in fruits and vegetables have shown to promote oral health by improving overall nutrition and microbiome profile^{1,2}.
- Among the many fruits, black raspberries (*Rubus occidentalis*) have shown in rodent and cell studies to improve oral health and prevent oral cancer^{3,4}.
- Clinical trials have shown mixed effects



¹Winn, D.M. *Am J Clin Nutr* 1995 Feb;61:437S-445S

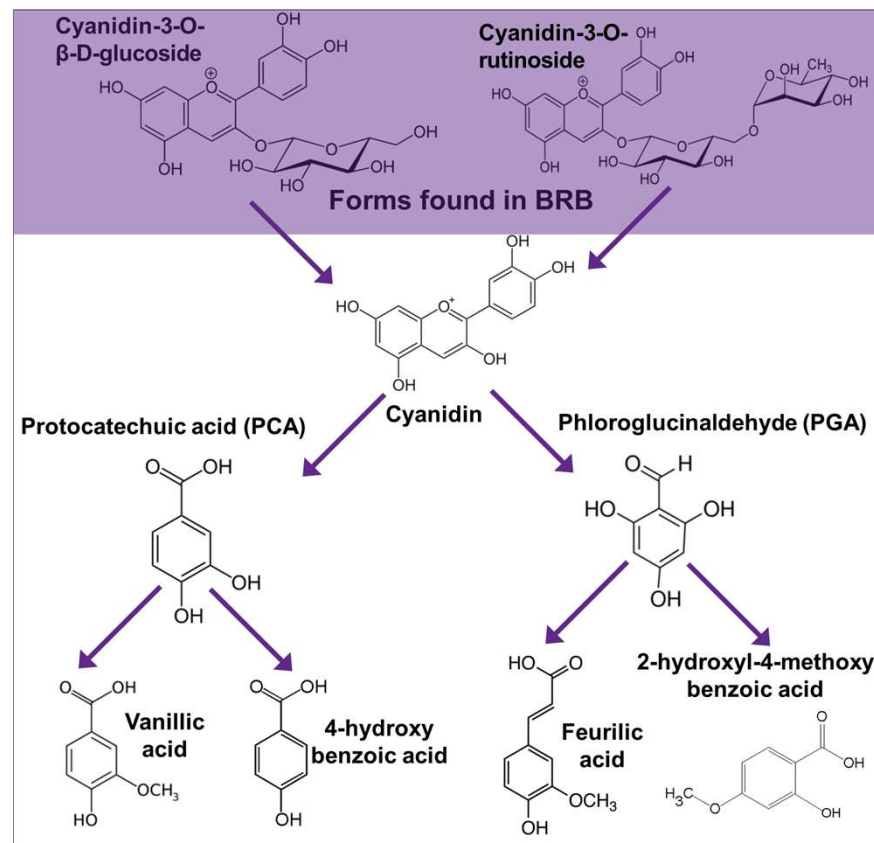
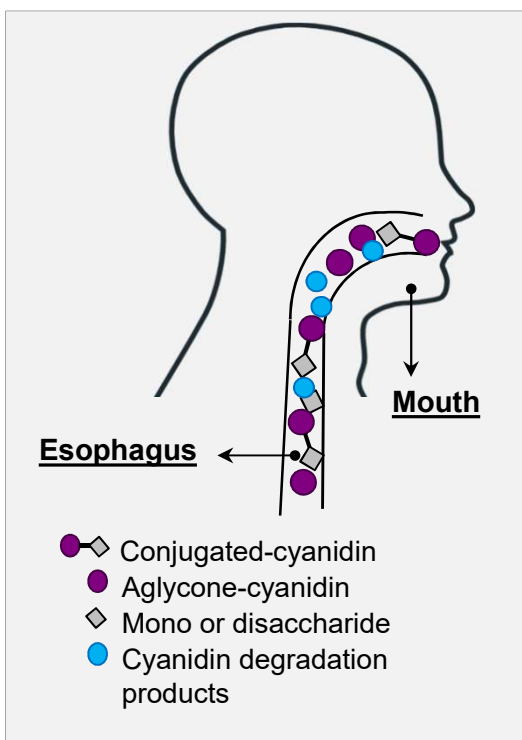
²Hezel, M.P. and Weitzberg, E. *Oral Dis*. 2015;21:7-16

³Casto, B.C. et al *Anticancer Res* 2002; 22:4005-15

⁴Mallery, S.R. et al *Cancer Prev Res* 2011; 8:1209-21

Oral Residence Time and Oral Metabolites

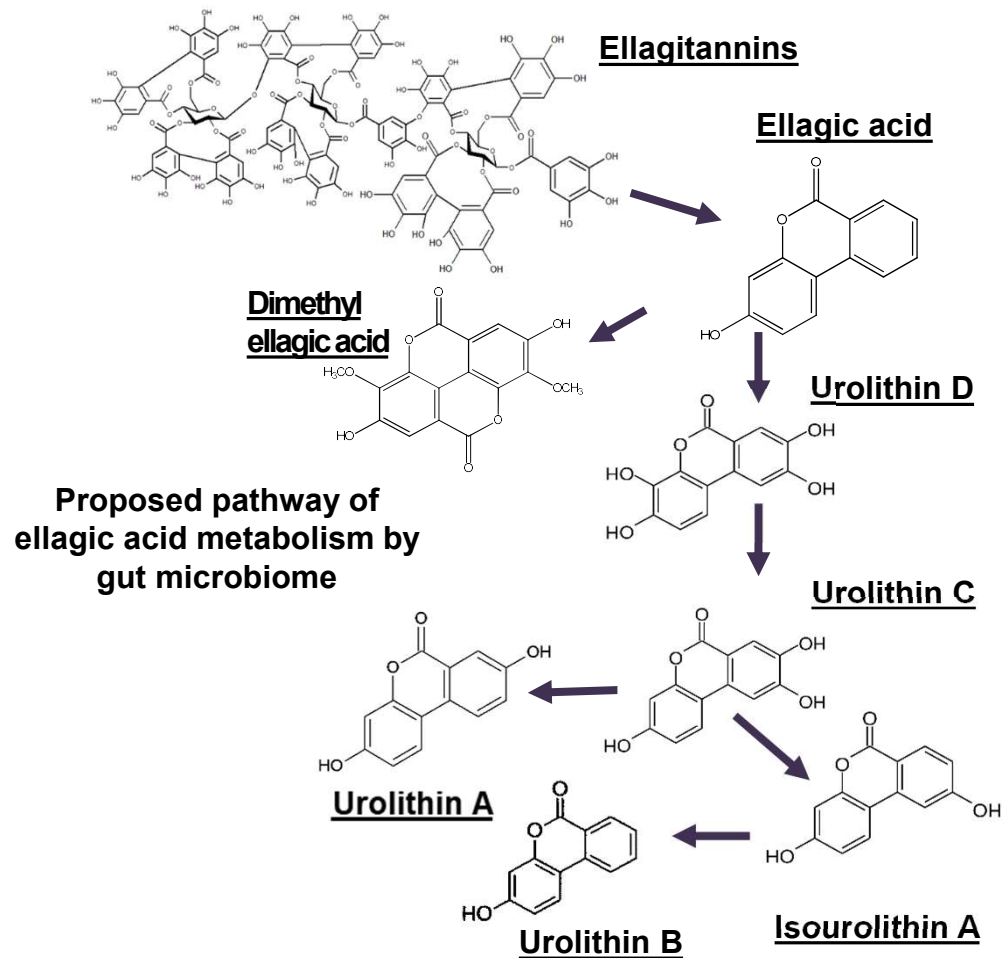
Enhanced Absorption vs. Enhanced Degradation¹



BRB: Freeze-dried black raspberries

¹Ahn-Jarvis et al *Cancer Res* 2014;74:19

Gut derived metabolites

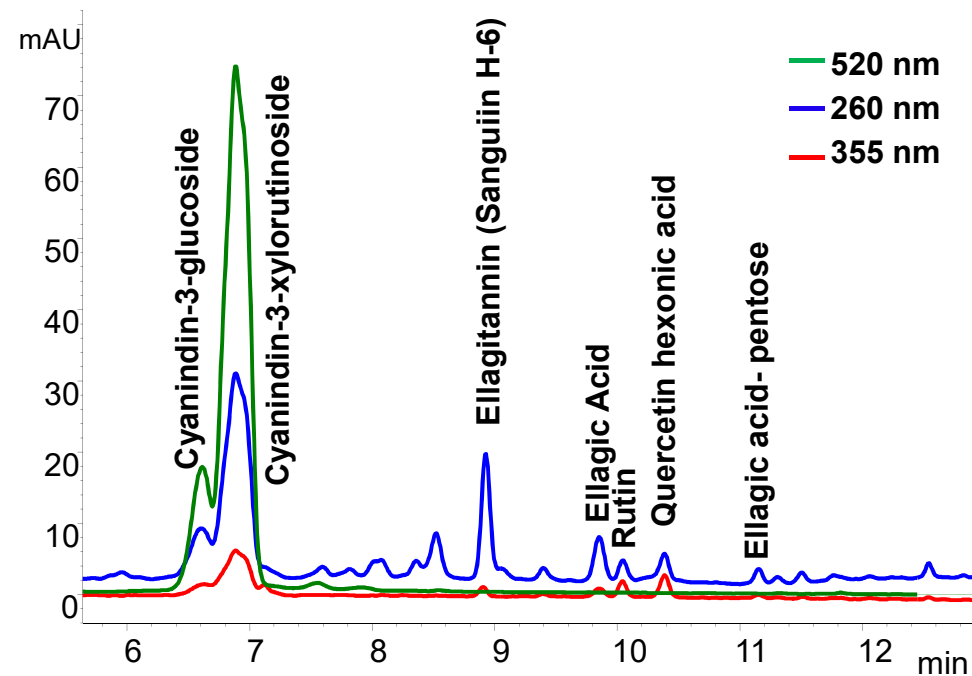


1. Tomás-Barberán et al *Mol Nutr Food Res.* 2017;61:1-35

Standardization of Black Raspberry Powder (BRB)



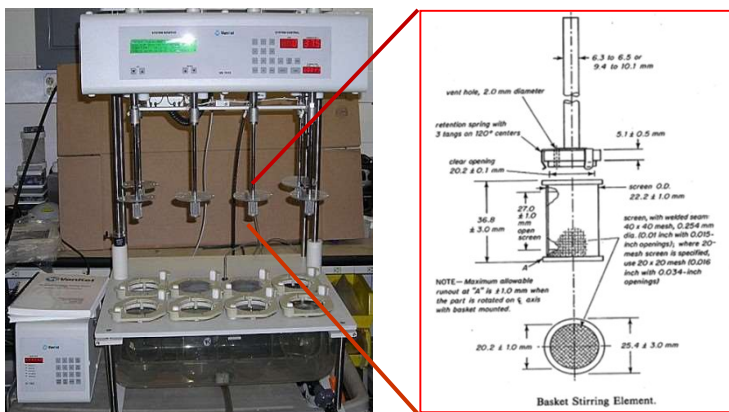
Large Scale Production Black raspberries were procured from Dale Stokes in Wilmington, Ohio (15 kg) and Berri Health, Oregon (6 kg).



HPLC chromatogram of BRB mixture after blending and peak identities verified using external standards and tandem mass spectroscopy¹

¹Gu et al *J Agric Food Chem.* 2014;62:3997-4006

Dissolution Apparatus to Approximate Oral Residence Time



USP I dissolution apparatus was used to determine oral residence time of various amorphous forms using PBS and synthetic saliva (100 RPM, pH 6.5 at 37°C)^{6,7}.



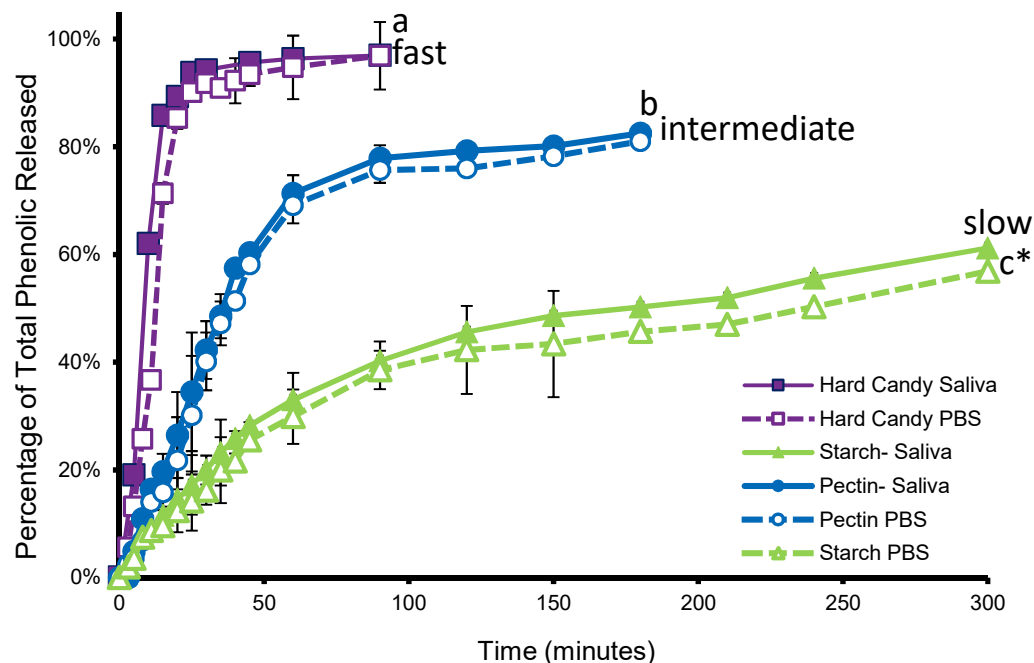
Hard Candy
(glassy)



Pectin
(visco-elastic)



Starch
(elastic)



Three amorphous forms show 3 distinct release behaviors¹

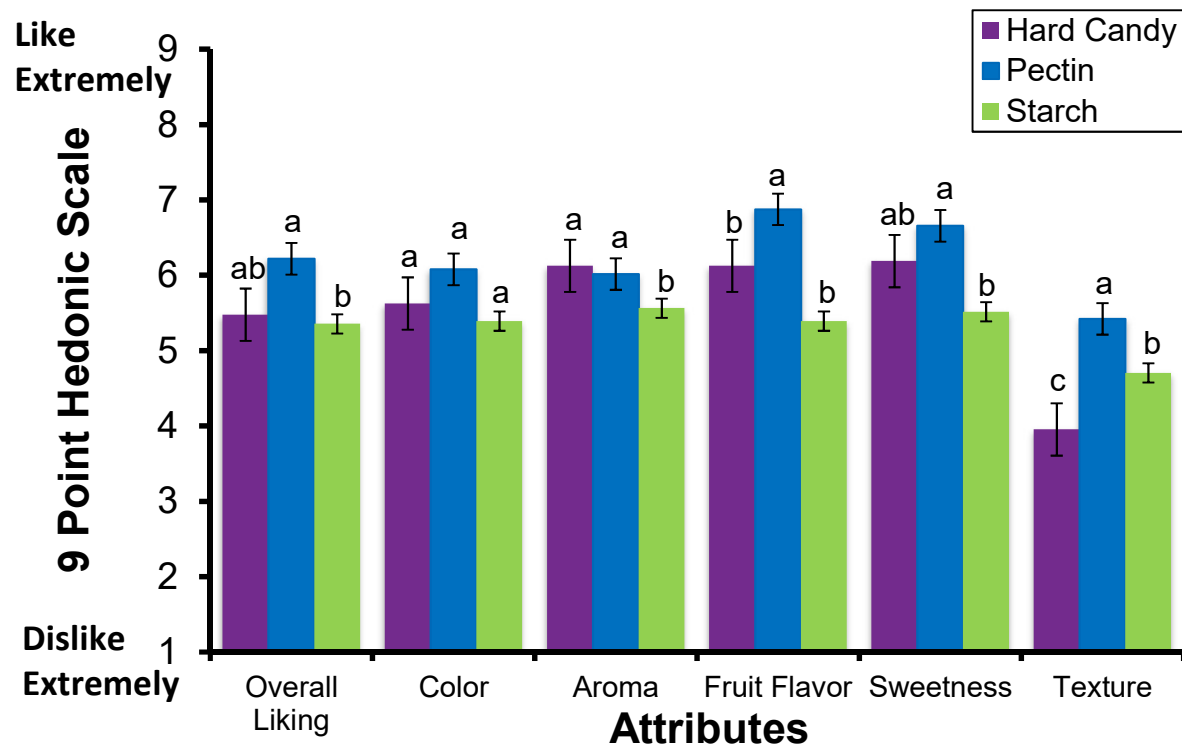
*Complete dissolution occurred at 600 minutes. Different letters denote differences in rate of total phenolic release using ANOVA ($p \leq 0.05$) with Tukey's posthoc test

¹Gu et al *J Food Sci.* 2015; 80:E610-8

Sensory Evaluation for Clinical Adherence and Optimization of Formulation



Sensory Evaluation confections conducted under sensory booth conditions (n=65). Letters denote mean separation where significant differences ($p \leq 0.05$) were found using ANOVA with Tukey's posthoc test.



Optimized Confection Formulations

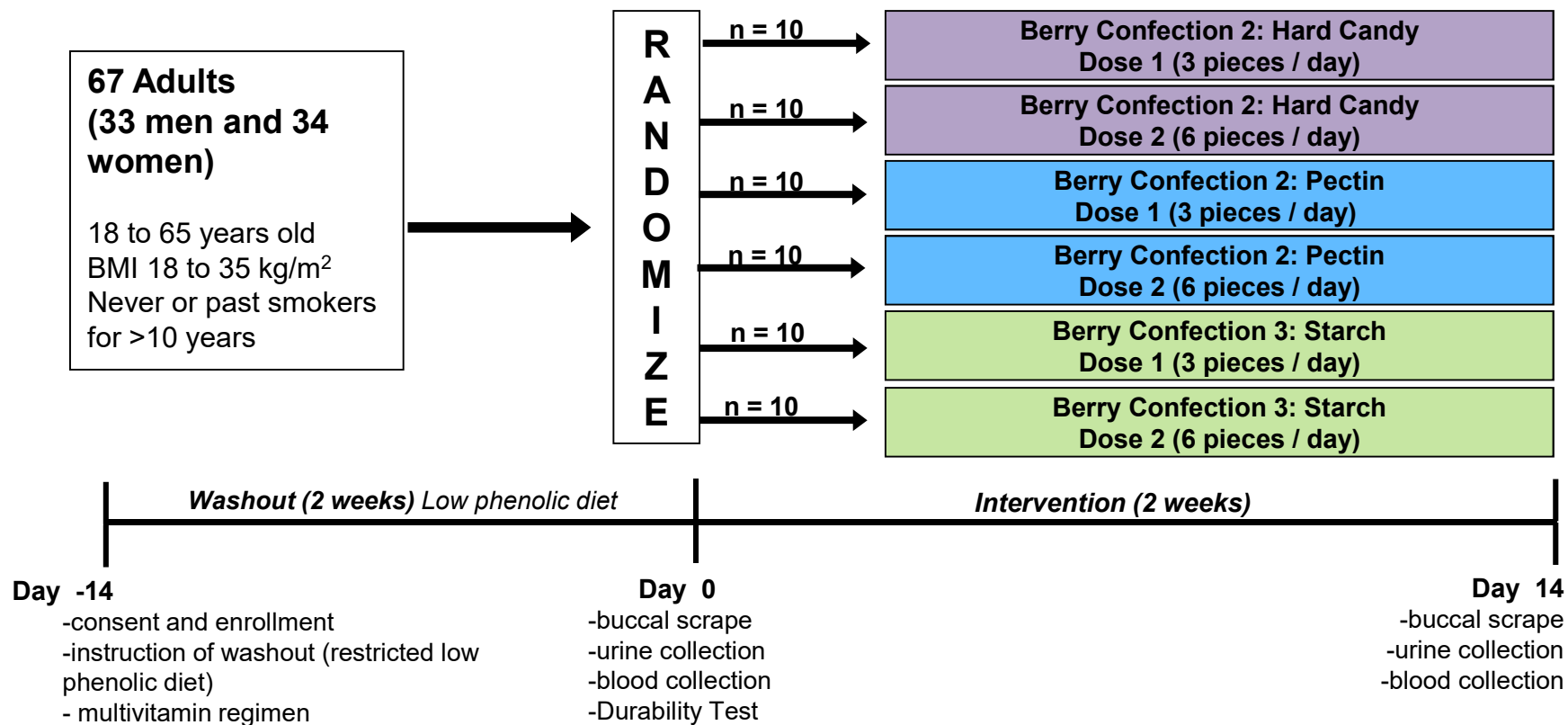
Composition (g)	Hard Candy	Pectin Confection	Starch Confection
BRB powder	1.25	1.25	1.25
Sugar	3.15	2.18	0.63
Corn syrup	1.85	0.75	2.28
Water	-	1.85	1.70
Starch/pectin	-	0.09 (pectin)	0.39 (starch)
50% (w/w) citric acid	-	0.13	-
Total	6.25	6.25	6.25

BRB: Standardized freeze-dried black raspberry powder

Starch: Tate and Lyle Confectioners G cornstarch

Pectin: Danisco Grindsted CF 130B

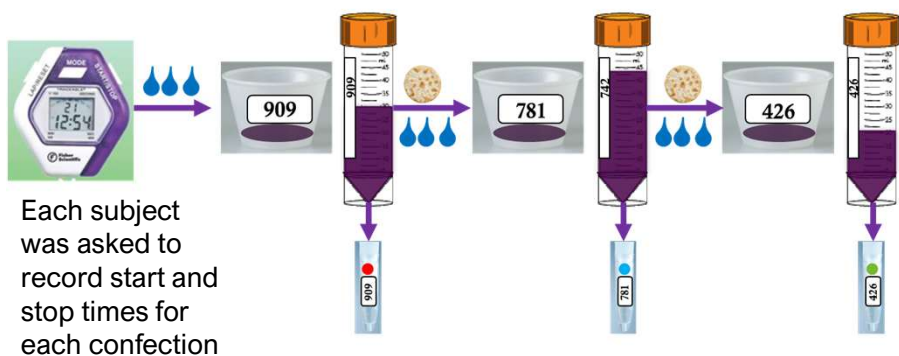
Study Design



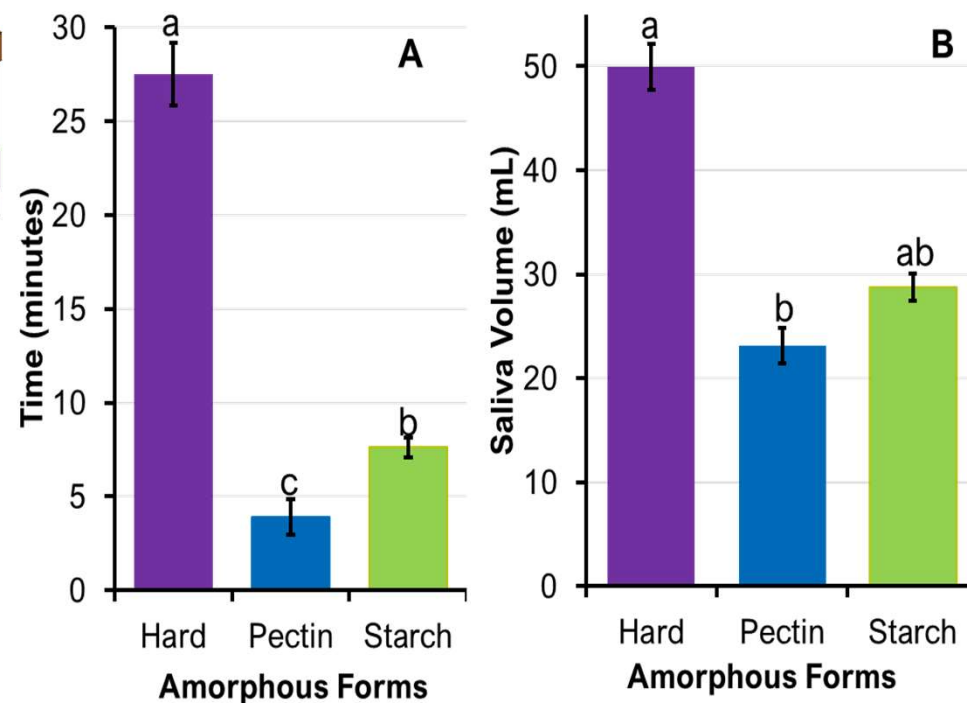
Demographic and Adherence Measures of Confection Study

Age (mean \pm SD)	33 \pm 11 years old
BMI (mean \pm SD)	26.6 \pm 9.2 kg/m ²
Compliance (mean \pm SD)	
Hard Candy	93.2 \pm 15.0%
Pectin	93.9 \pm 12.8%
Starch	96.4 \pm 12.3%
History of dental surgery	13% (9/67)
Twice daily teeth brushing	66% (44/67)
Daily flossing	69% (46/67)
Regular alcohol consumers (average 3.25 servings/ week)	69% (46/67)
Never smokers	89% (60/67)
Past smokers (0.5 pack/ 5.5 years)	11% (7/67)

Oral Residence Time (Assessment of Confection Durability)

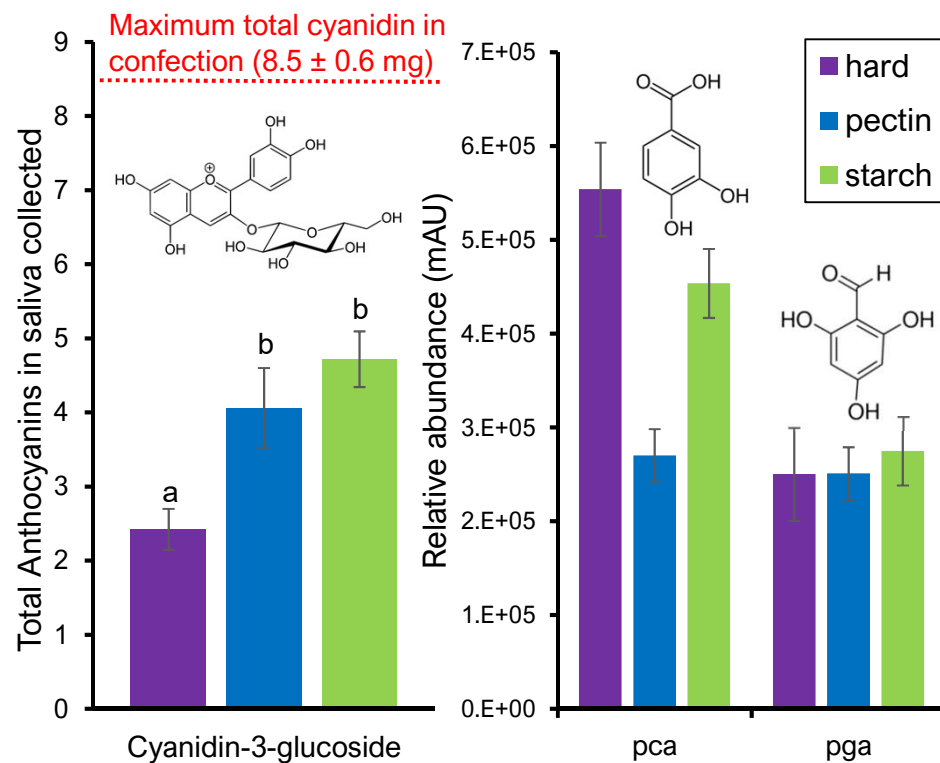


- Three confections were administered in a randomized crossover design during a single visit.
- Participants were instructed to vigorously tumble confection but prohibited from chewing confection.



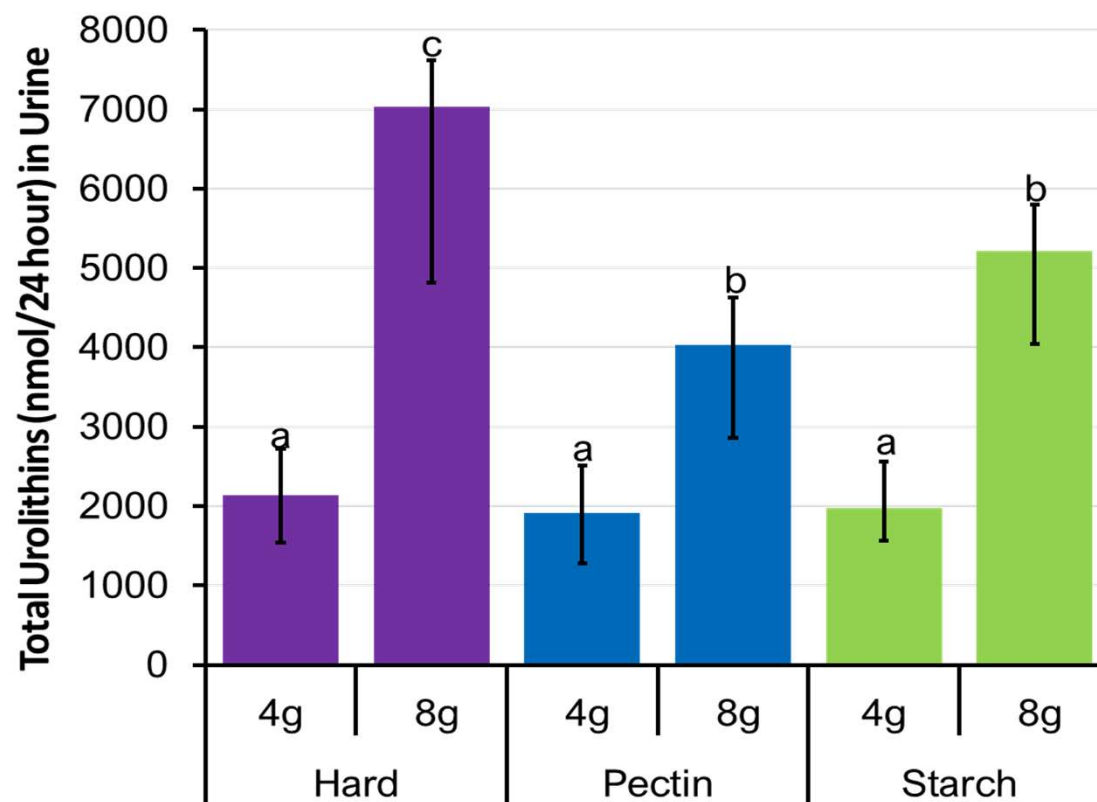
*Oral residence time in minutes (A) and quantity of saliva produced with each confection (B). Letters denote differences using ANOVA ($p \leq 0.05$) with Tukey's posthoc test

Salivary Metabolites



Different letters denote significant ($p \leq 0.05$) differences using ANOVA with Tukey's posthoc test

24 hour Total Urolithins



- 3 confections at two doses (4 and 8g/day) consumed for 14 days (n=62).
- Total urolithin reflects urolithin A to D and isourolithin A.

Different letters denote mean separation where significant differences ($p \leq 0.05$) were found in total urolithin in 24 hour urine using ANOVA with Tukey's posthoc test

Conclusions

1. **Oral residence time:** hard candy was the most durable having longest oral residence time resulting in the greatest volume of saliva
2. **Salivary metabolites:** cyanidin-3-glucoside significantly less during hard candy consumption but ellagitannin and ellagic acid increased.
3. **Huge inter-individual differences** observed in the rate of confection consumption, quantity of saliva produce, and polyphenolic profile
4. **24 hour urine:** No differences in total urolithins excreted with 4g dose but significant differences were observed between pectin and hard candies with 8g dose of BRB suggesting that confection matrix may impact ellagic acid metabolism

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