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Using Salivary Analysis to Confirm the Presence of Metabolites

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Abstract: *The deficiencies of current diagnostic tools for Addreall are analyzed. A Java-applet was developed which analyzes delta E values from the Color Catcherapp by TECHKON. This app is particularly useful for takingapictureof thecolorchangefrom thereaction and then quantifyitthrough adelta E value. Further the Java-appletanalyzes deltaEvalues,which are collectedforthe controls for eachexperimental samples.The values can be typed into Java applet as inputs. A comparative study is made between, several student saliva samples, againsttheir respectivecontrols. The applet compares metabolites in the experimental saliva against the metabolites in the respective control saliva, and finally provides meaningful conclusions. This applet help removing the possibility for any human error, and is thereby useful as an objective decision making tool.*
Keywords: *Adderall, deltaE, saliva, chromophore, Hydroxyamphetamine, b- endorphin, DOPAC*

I. Introduction

The past and current research on diagnostic tools for Adderall, does not throw sufficient light and reliableconclusions about the patient.Primarily this is so due to human error which occur during data collection and data analysis of urine samples. Furthermore, the instrument used in urine analysis, GC-MS consumes immense time and energy. In addition, the methodsrequiringurinesamples need patients to be alone, whensamples can be altered. Sputumsamples areinconclusivesincetheyanalyzeonlyonemetabolite which maynot even occur.Blood testsposeasafetyhazard which requires alaboratoryenvironment.

With the creation of an easy to use saliva drugtest, the abuse of drugs would greatly decrease. Currently, the diagnostic tools for drug testsdo not provideneither reliable nor immediateconclusions about the patient. With a sputum drug test, the identification process for drug abusers would be more efficient. Furthermore, themethodologyof analyzingdeltaE values usingaJava-applet whichcompares experimental sampleto the control can not onlybeused to diagnoseAdderallin saliva, but also can beused to diagnoseheroin, cocaine orotherdrugs found in saliva.If theright biomarkers arefound, this methodologycan beused to detect anydrugin saliva. Before we go into the details of developed Java applet, let us have a look at Adderall as a central nervous system stimulant.

1.1 CENTRAL NERVOUS SYSTEM STIMULANT: ADDERALL

Adderallis a powerful central nervous system stimulant, oneof themost common commonlyabused psychostimulant drugs. Adderallis a specifictypeofamphetamine. Amphetamine areagroup of central nervous system stimulants known for their indirect effects on the central nervous system and peripheral nervous system. Adderallwasfirst introduced as an effectivemethod for treatingthe symptoms of narcolepsyand attention deficithyperactivity disorder (ADHD). However, dueto thefact Adderallis oneof thefew stimulants which arelegal in America, itis also oneof themostcommonlyabused drugs.(Becker, 2015). In general, Adderall is commonly used to treat the symptoms of deficit hyperactivity disorder (ADHD), as shown in below Figure 01.

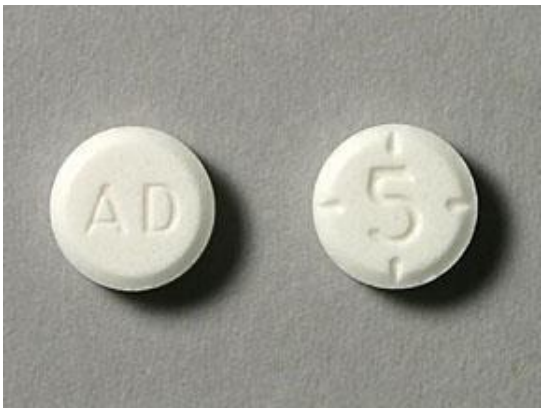

Figure 1: Adderalltablet(Rivers)

1.2 ATTENTION – DEFICIT/HYPERACTIVITY DISORDER (ADHD)

Current research suggests that ADHDis associated with functional impairments in some of thebrain's neurotransmitter systems [xyz]. Thesefunctional impairments are usuallydistorted dopamineneurotransmission and norepinephrineneurotransmission involved withthe brain's physiological responses to stress and panic. Psychostimulants such as amphetamineincrease neurotransmitter activityin thebrain, repairingtheimpaired dopamineneurotransmission andnorepinephrine neurotransmission. These extradopamine andnorepinephrineneurotransmitters increaseimpulse controland attention span; therefore, theyareconsequentlyusedas medication forADHD, as shown below in Figure 02 [Olmez, 1988].

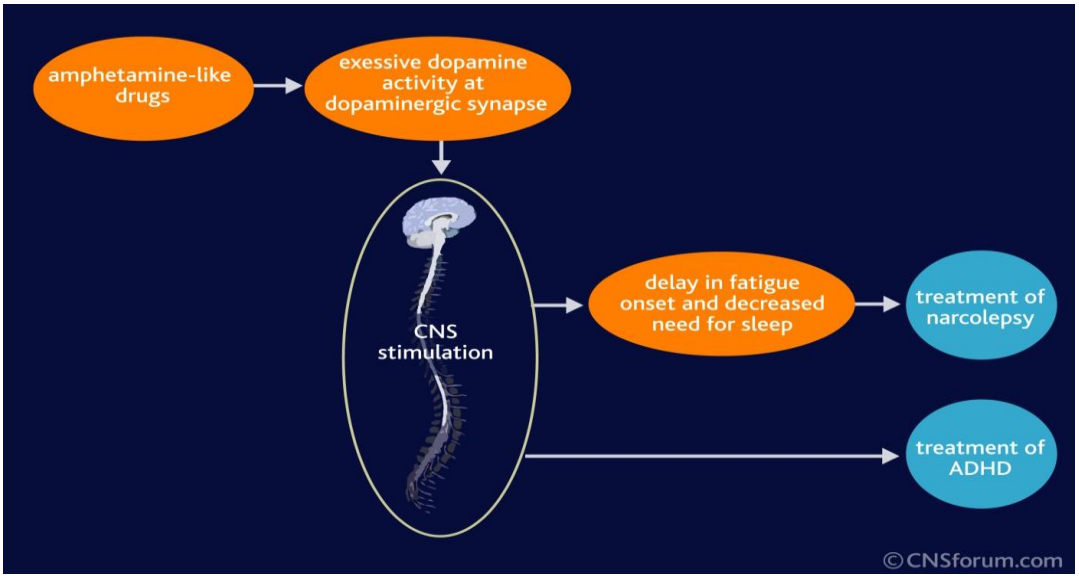

Figure 2: Diagramofhow Adderall's effects counter the effects of ADHDand narcolepsy(Olmez, 1988)

1.3 SOME FACTS ABOUT ADDRELL ABUSE

Since amphetamines behavelikedopamine, theyalso havetheabilityto bind to the same enzymesas dopamine, and can releaseeuphoria. Furthermore, theincreasein euphoria and expanded attention span, makeAdderalloneof themostcommonlyabused drugs amongstudents. Abuseof amphetaminemedication, such as Adderall, is a concern oncollegecampuses. Students abuseAdderallformanyreasons, however, it ismostlyused forimprovingattention to do help improvegrades. Some other common reasons to abuseAdderallincluderecreational use, and reducinghyperactivity [Olmez, 1988], show in the below Figure 03.

TABLE 1. Sample and Population Demographics, in Percentages

Characteristic	University (N = 11,897†)	Total sample (N = 1,025)	ADHD diagnosed students (n = 68; 6.6%)
Age (y)			
17	< 1	< 1	0
18	16	24	22
19	19	19	24
20	18	18	12
21	16	17	13
22–23	12	11	7
24+	19	11	22
Female	58	66	52
Year in school			
Freshman	22	31	32
Sophomore	22	20	19
Junior	20	19	16
Senior	20	21	25
Graduate	19	10	7

†From *University of New Hampshire 2001 Fact Book*. University of Hew Hampshire Office of Institutional Research. Available at: http://www.unh.edu/ir/master_factbook_01PDF.pdf. Accessed July 15, 2004.

Figure 3: Table which demonstrates the number ofstudents attheuniversityofNewHampshirewho use Adderallandthosewhoactuallyneedit.(Olmez, 1988)

Therecent studycollected data in patient students' ofpeople who used Ritalin, Adderall, Cylert, Dexedrine, Concerta, oranyother stimulant medication. This was an onlinesurveyto be sent to the students of New HampshireUniversity.It wasconcluded that 95.4% ofthe students can be concluded that wereonastimulant medication illegally.

This study emphasizes not onlythe college students but alsothe truck drivers who arealso known to be common Adderall abusers. Amphetamineis themostcommonlyconsumed drugbytruck drivers. Urinesamples of Mexican truck drivers wereevaluated.In arecentstudy, 109 hadamphetamine(90%) and 12 had methamphetamine(10%). Themetabolite 4-hydroxyamphetamine wasalso tested for, and thosewhich tested positiveforitwerequantified in theamphetaminepositivegroup [Barceloux,2012], as shown below Figure 04

Table IV. Results of Urine Analysis of 121 Subjects (100%): 109 Amphetamine Positives (90%) and 12 Methamphetamine Positives (10%)

Amphetamine in Urine Range (ng/mL)	Number of Individuals	Methamphetamine in Urine Range (ng/mL)	Number of Individuals	4-Hydroxyamphetamine in Urine Range (ng/mL)	Number of Individuals
1000 to 5000	19	1000 to 5000	1	0 to 500	26
5000 to 10,000	44	5000 to 10,000	4	500 to 1000	25
10,000 to 20,000	33	10,000 to 20,000	4	1000 to 2000	30
20,000 to 50,000	12	20,000 to 50,000	2	2000 to 5000	18
> 50,000	1	> 50,000	1	> 5000	10
Total	109	Total	12	Total	109

Figure 4: Table which displays the Amphetamine,Methamphetamine ,and4-Hydroxyamphetamine levels inthe urine of TruckDrivers.(Barceloux,2012)

1.4 PHARMACOKINETICS

Pharmacokinetics is thestudyof howAdderallis metabolized in thebody.Adderallis primarily metabolized in theliver. To form 4-hydroxyamphetamine, amphetamineis either oxidized at thebenzeneringto form alpha-hydroxy-amphetamine. Or, it isoxidized on the side chain of ß carbons sideto form norephedrine. Norephedrine and 4-hydroxyamphetamineare both metabolites of amphetamine and areboth oxidized to form 4-hydroxyl-norephedrine. Then the alpha-hydroxy-amphetaminegoes through deamination to form phenylacetone. Phenylacetone thenforms benzoic acidand its gluronide and theglycineconjugate hippuric acid; however this is a common reaction ofphenylacetone; it is not specificto amphetamine metabolism. CYP2D6, dopamineβ-hydroxylase,6 lavin-containingmonooxygenase3, butyrate-CoA ligase,andglycineN-acyltransferasearetheenzymes that metabolizeamphetamine [Chaing, 1986], as shown below.

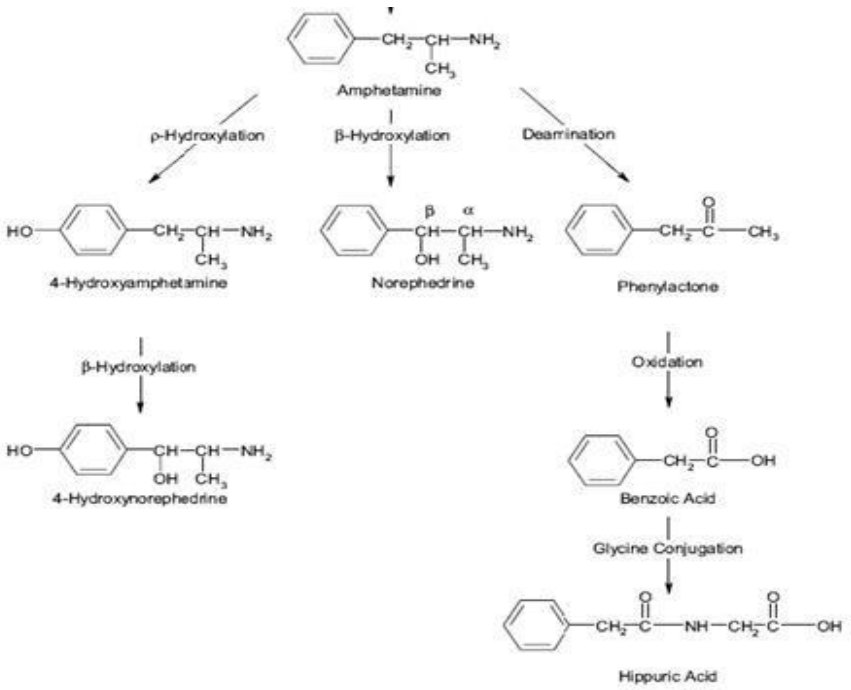

Figure 5: MetabolismofAdderallin body (Chaing,1986)

Thegastrointestinal pH determines the oral bioavailabilityofamphetamine.If amphetamineis wellabsorbed from theliver, then the oral bioavailabilityis over75%for dextroamphetamine. Amphetamines are aweak base. ThepKais about of9–10. When the pH is morebasic, moreof thedrugis in its lipid solublefreebaseform. This allows moreof amphetaminetogetabsorbed throughthe lipid-rich cellmembranes of theliver. It is realized that 15–40%of amphetaminein thebloodstream is bound to plasmaproteins [Becker, 2015].

1.5 MAJOR EFFECTS OF AMPHETAMINE

Themetabolites of amphetamine, *d*- amphetamine(*d*-AMPH) and *l*-amphetamine(*l*— AMPH), are reversiblemonoamine oxidasetypeA inhibitors. Reversible inhibitors of monoamine oxidaseA (RIMAs)are a class of drugs whichareveryselective ofthe enzyme monoamine oxidaseA (MAO-A)that theychooseto reversiblyinhibit. Monoamineoxidasetype A (MAOA)inhibitors are an enzyme encoded bythe MAOAgene. Thehuman bodyhas two neighboring genefamilymembers that encodeformitochondrial enzymes.MAOA is oneof the two.It catalyzes the oxidative deamination of amines; for example, serotonin, dopamine, and norepinephrine.Becauseof their reversibilityandselectivity, RIMAs aresafer than monoamineoxidaseinhibitors (MAOIs) likephenelzineand tranylcypromine, as shown below

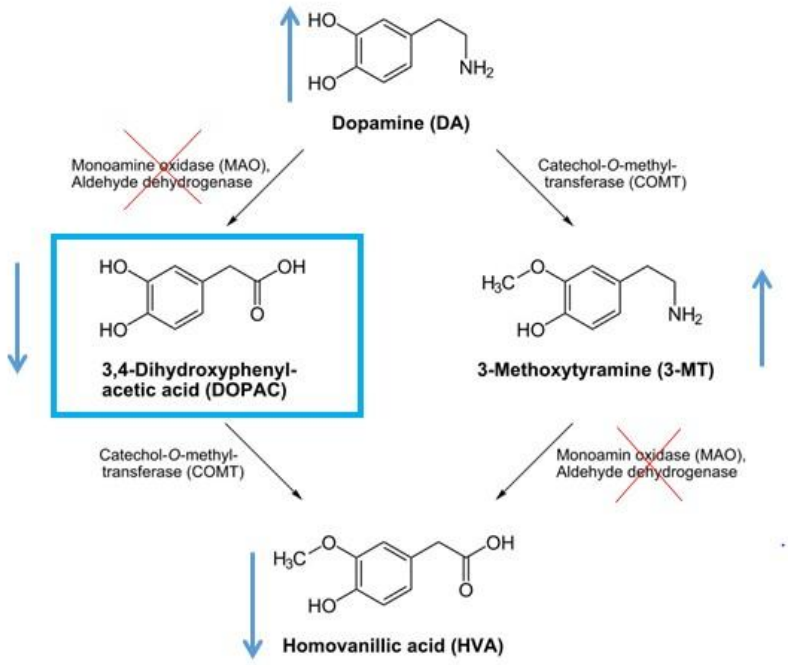

Figure 6: DiagramofhowDopamine levels areaffectedwithAmphetamine

Some knowmolecules areknown to increasetheconcentration ofthe ionized species of the amphetaminemolecule. This increasein amphetamine's ionized speciesincreases urinary excretion. Thesemolecules also lower blood levels and efficacyof amphetamines. Some ofthe known molecules includeammoniumchloride, sodium acid phosphate.(Gulovali, 1988). Amphetamines also inhibit adrenergic antagonist.Adrenergic antagonistisa pharmaceutical substancewhich inhibits catecholamines, agroupof monoamines which have specificphysical organiccompound properties. These adrenergic antagonists inhibit catecholaminesat the adrenergicreceptors. Similar to mostpharmacological receptor antagonists, the receptors'effect can onlybeseenwhen the receptor's effector is present.

Furthermore, amphetamines havethe potential toenhancethe activityof tricyclicor sympathomimetic agents.When the metabolited-amphetamineis exposed to desipramineor protriptyline and possiblyothertricyclics, itincreases the concentration ofd-amphetaminein the brain. Consequently, thecardiovascularsystem has the potential to be effected.(Gulovali, 1988)

1.6 CHROMOPHORES

Chromophores are compounds that are produced the color in dyes. Theyabsorb electromagneticradiationof different wavelengths, which depend on theenergyof theelectron clouds, to produceacolor. Chromophores arestructures with atoms joined in a sequence composed of alternating single and double bonds.Chromophore configurations often existas multiple units, havingconjugated doublebonds, and aremore effectivewhen theydo so. This is dueto theinteraction between the doublebonds,which causes partial de-

localization ofthe electrons involved in thebonds.In this case, although specific atoms areinvolved in the bonds, the electronsaredistributed over alarger areathanthe specificatoms and also involve adjacent atoms that havedouble bonds(Rivers, 2015) . Thepointof this is that conjugated systems have partiallyde-localized electrons, and the energyin thesede-localized electronscan impact on theenergyof thede-localized electrons ofthe parent aromatic compound byextendingthe number of electrons involved in thesystem andtheenergyneeded to keep thewholesystem in place.

1.7 EXISTING TEST STRIPS& SAMPLE COLLECTION

Thetest deviceconsistsof achromatographicabsorbent devicein which thedrugor drug metabolites in thesample competewith a drug conjugate immobilized on aporous membrane support for thelimited antibodysites. As the test sampleflows up through the absorbent device, the labeled antibody-dyeconjugatebinds to thefreedrugin thespecimenforminganantibody: antigencomplex. This complexcompetes with immobilized antigen conjugatein thepositive reaction zone and willnot produceamagenta color band when thedrug(SalivaConfirm), as shown in the below Figure 06.

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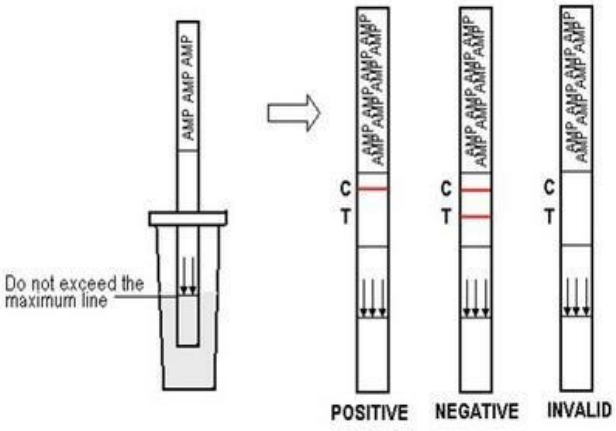

Figure 7: Illustrationofcurrentsaliva teststrips(SalivaConfirm)

It is also important to realize, that thedeltaE value is primarily based on an algorithm originallydeveloped byRichardHunter in1972 which is based on 3dimensional Euclidean differenceformulae(equation 1) that takes theroot ofthe differenceof the color coordinate squares based onthe standardCIELAB color axis [Fairchild, 2005]. Ifcoordinate1 is (x1,y1, z1) and coordinate 2 is (x2,y2,z2), then the value of delta E can be easily calculated using the below formula

$$\Delta E = \sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2 + (z_1 - z_2)^2}$$

This calculation ofdeltaE is widelyused in printingand photographyas itprovides as common platform for costumers, printproviders and suppliers to exchangetheirresources andrequests.
[Fairchild, 2005], as shown below

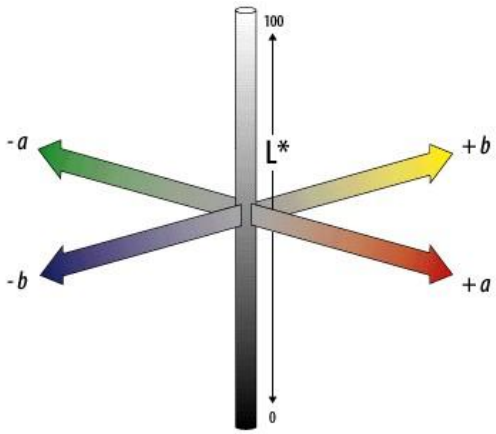

Figure 8: CIELAB Coloraxis.Delta Eis calculatedfromtaking2pointsonthis3D coordinate systemand thendefiningx,y,zaccordingtothe coloraxis as shown here.These axes are defined based onthe simple theorythat notwocolors canbe the same identical partsofredand green, blue andyellow,and black and white.(Fairchild, 2005)

Thenumerical values used in theformula come from the color-modellingsystem devised byAlbert HenryMunsell.In his 1898 publication"A Color Notation" hedescribes color using a decimal system as opposed to adjectives.(Fairchild, 2005) His work remains a standard for colorimetryeven todayand has been adopted even in this numberingsystem bywhich deltaEwas calculated.

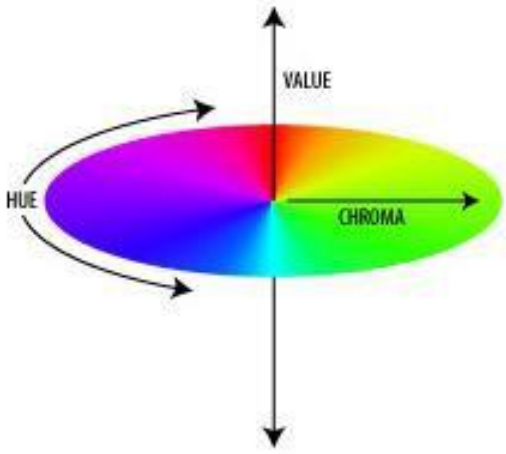

Figure 9: Overall model of Munsall. Munsell'smodelisbasedona 3D sphere where the centralslice (termedequator)carries a bandofcolors andthe verticalaxis runningperpendicular tothis slice is the gray scalewith black andwhite ateither pole.Movingoutwards fromthe center towards the outside alongthe samegraypoint(same pointonthe verticalaxis) provides differentlevels ofsaturation.(Fairchild, 2005)

1.8 UNDERLEYING ENGINEERINGPLAN
In this research we propose an engineering plan, detailed below, setting up fixed goals and certain procedures.

A. Engineering problembeing addressed:
Currentlyno definitivetestsforAdderallusein classrooms exist. Methodsrequiringurine samples need patients tobe alone, wheresamples can bealtered. Sputumsamples are inconclusivesincetheyanalyze1 metabolite thatmaynot occur.

B. Engineering Goals:
Thegoal of this project is to engineer amethodologyofanalyzingdeltaEvalues using aJava- applet that compares experimental sampleto thecontrol.

C. Detailed Description of the involved procedures:
Procedures:
Each colorchangingmolecule (b-endorphin, DOPAC, and Adderallmetabolite)willbepaired with its respective(chromophore) to createan invisible color change. When allthreeinvisible distinct color changes happen, anothercolor will be formed. This colorwillonlybeformed if all threecolorsarepresent,which willindicate Adderallis present in saliva. TheQualified Scientist willdo the chromophores pairingin his lab.

Data Analysis: Mysalivawillbe collected and tested byplacingthe chromophoretest strip as a control. TheQualified Scientist will putthe threeAdderallmetabolites (CYP-450 metabolite,
3,4-Dihydroxyphenylacetaldehyde, and b-endorphins) in theothersampleof mysaliva,and test the strip again.
Design Criteria and SecondaryEngineering Goals: Thetest strip should onlymakea color if Adderallis present in saliva. Nothing else in salivashould influencethat color change. Furthermore, mytest strip's reactions should beindependent ofallothersubstances in saliva.
Testing: Mysalivawillbeused as acontrol. Common elements of Adderall influenced saliva includingCYP-450 metabolite, 3,4-Dihydroxyphenylacetaldehyde, and b-endorphins willbeput into anothersampleof mysaliva, in a lab environment.

II. Research Methodology

In this research, we have developed a research methodology which is more practical and significant, especially with reference to time effectiveness. TheColor Catcherapp byTECHKON© was usedto captureapictureof thesputum color with theLEDlightturned on. ThegeneratedDeltaE value was compared to theprovided "normal" and"Adderallabuse' samples. Sincethelightingand iPhonecameralens maybe different, thenormal and"Adderallabuse"samples areprovidedso theperson collecting samples willbe able to usetheirown

phonetogenerate thenormal and"Adderallabuse" controls underthe sameconditions as the samples being collected.

OncetheDeltaE values are collected for the controls,theycan betyped into the respectiveinputboxinthe Java-applet. Thesewillfunction as theparameters for howthestudent's samples willbe evaluated. As the pictures of students samples aretaken usingthe app, thedeltaE valuecan betyped into the respective input area for collected samples as along with the corresponding user interface for the app created by the author is shown below:

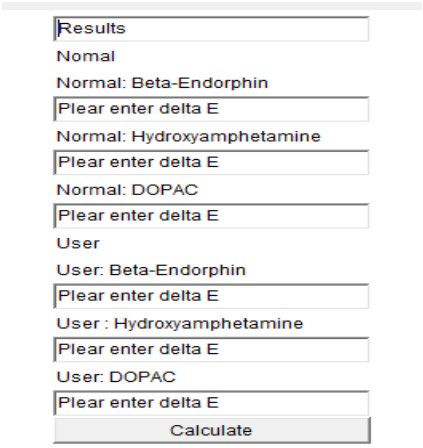

Figure 10: User Interface for the app.

Digital recordingof thedata will protect the authenticityof thedata collected and enable immediate sharingof thedata for futurerecords. The applet willgenerate aconclusiveresultof whetherthe student maybeapotential Adderalluser ornot.Iftheresultsuggest that thestudent's color changeswereout of thenormal range, then the next step would beto placethem in a monitored settingfor24 hours wheretheywillbe allowed to eat, drink and rest normallybut then tested again just asbefore.If theresults come to besimilar to thefirst timethen it showsthat the patient is not usingAdderall, but if therearedistinctive different color changes providing different DeltaE values,then it maysuggest thesefluxuations maybewithdrawal effects of not havingthe drugforafull24 hours.

III. Experimental Results

(ug/mL)	b-endo	4-HA	DOPAC	
Color	Orange	Blue	Green	
1	48.5	0.35	0.98	ADD
2	55.3	0.7	1.1	
3	49.2	0.23	0.87	
4	48.3	0.65	0.96	
5	55.7	0.34	0.99	
6	56.4	0.21	0.92	
7	47.9	0.57	0.95	
8	54.8	0.76	0.9	
9	49.8	0.11	0.92	
10	48.4	0.81	0.88	
Average	51.43	0.473	0.947	
SD	3.6043338	0.25408	0.0671731	
(ug/mL)				
Color	not Orange	Not Blue	Not Green	
11	44.3	0	1.33	CLEAN
12	50.2	0	1.35	
13	47.4	0	1.29	
14	45.8	0	1.15	
15	52.2	0.01	1.17	
16	49.9	0	1.19	
17	45.5	0.04	1.05	
18	52.3	0	1.07	
19	51.1	0	1.51	
20	44	0	1.42	
Average	48.27	0.005	1.253	
SD	3.2421015	0.012693	0.1515879	

Figure 11: Table thattakes noteofthe PatientNumberandwhatitsdelta Eis forHydroxyamphetamine, b-endorphin,andDOPAC.

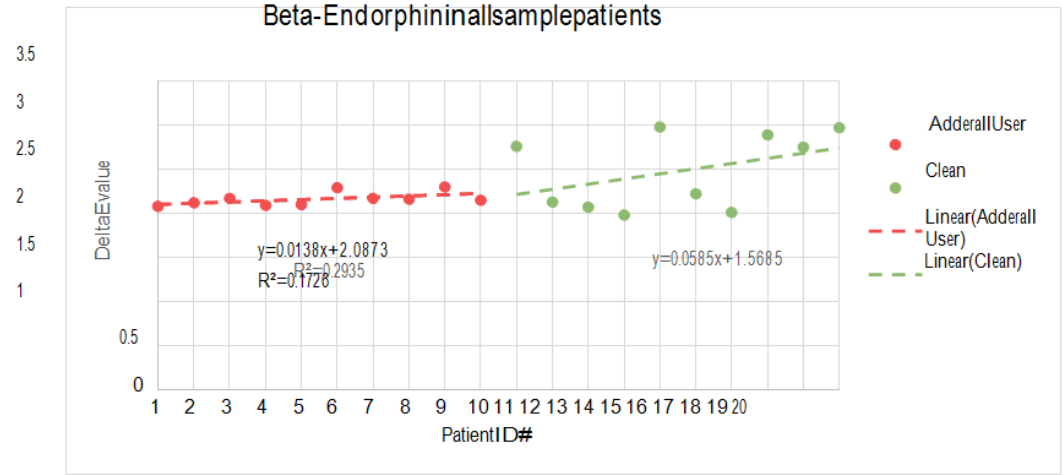

Figure 12: Graph of Delta Evalues ofBeta-endorphin levels inthe saliva ofPatients

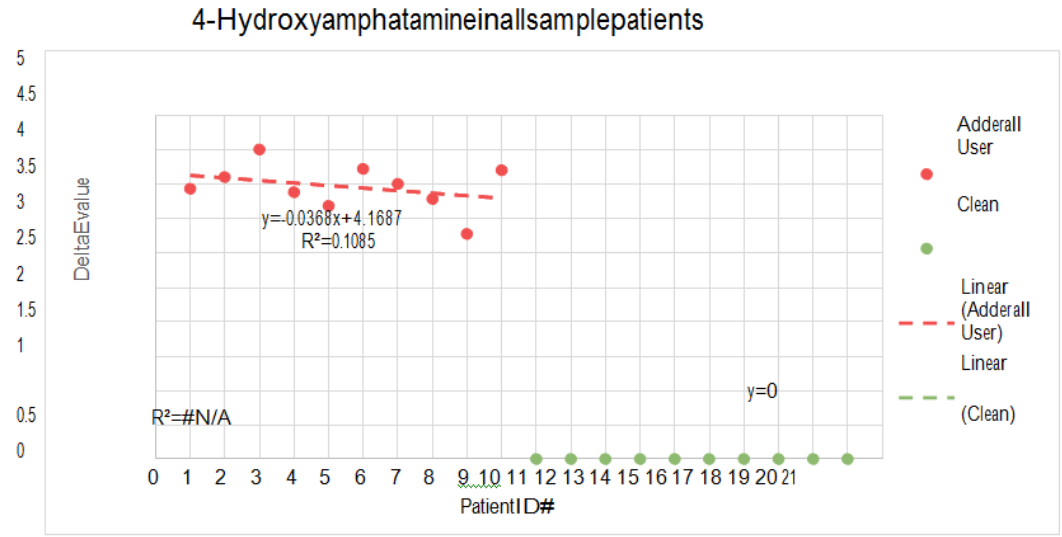

Figure 13: Graph of Delta Evalues of4-Hydroxyamphetamine levelsinthe saliva of Patients.

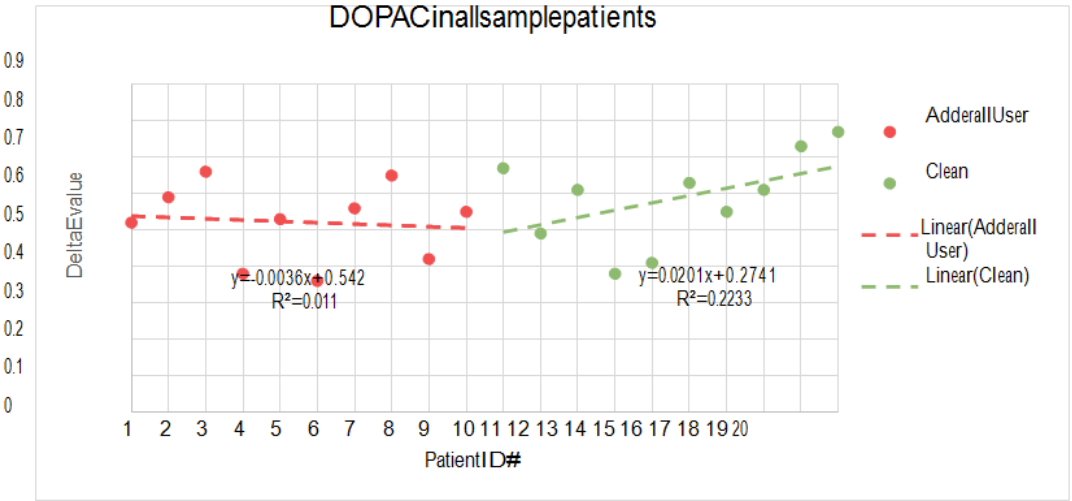

Figure 14: Graph ofDelta Evalues ofDOPAC levels inthe saliva ofPatients.

IV. Research Experimental Analysis

A particular research experimental analysis is detailed below to meet the goal of this project.It is basically an engineered methodologyof analyzingdeltaE values using aJava-applet that compares experimental

sampleto the control, andhaveused Adderallasan exampleto explain mymethodology.

The ΔE values from all sample patients were used togeneratethreeseparategraphs for each of thethreemetabolites: Beta-endorphins (b-endo), 4-Hydroxyamphatamine (4-HA), and DOPAC. ByplottingAdderallusersas wellas clean patients on the samegraph, itbecomes visuallyevident how differentlythe chromophoresreact to theirsputum metabolites. TheR^2 values for allof thegraphs depict apoorlinear regression. This, in combination to veryslight slope apparent on all thescatter plots, points to the fact that thereis no relationship between the patientID #'s and their respectivemetabolite values.When theseΔE values areinputted into the JAVA applet, the fact that they are individual values not dependent on anyothervariable enables the algorithm to producea conclusive and definitivestatement about themetabolites present.

Thetrends between the sputummetabolite plot and the ΔE plot aretrendingvery similarly, confirmingthestrongcorrelation between the collectedΔE valuesfrom the color changingreaction in thesputum and the actual metabolite content in thesputum. The JAVAappletenables this easilyadministered test outsideastandard laboratorysettingto be helpful in definitivelyidentifyingstudents who might be takingAdderallwithoutaprescription.

Thestandard deviation (SD)reveals that thevarianceof thedata valuescollectedwas low and the overallprocedure of data collection was reliable.In thesampleserum studies, theSD
was smallest in the 4-HAand DOPAC data values forboth Adderallabusingpatients aswellas clean patients. This shows that thedata collectionmethod of theb-endo was not as reliable as the datacollection method ofthe other 2 metabolites.This findingis supported bypriorliterature becausebeta-endorphinsarefound ineveryone ata constant amount. But dependingon the lifestyle factors of theindividual: athletic nature,proneto depression, andof courseuseof recreational stimulants, the amountof b-endo maybeslightlyhigher orlower. Theoverallserum averageb-endo for sample clean patients was 48.27 ug/mLwith an average Δ E =2.476, indicatingalight orangecolor. Theoverallserumaverageb-endo for Adderallusers was 51.43 ug/mLwith an average ΔE=2.163, indicating abright orange color. Theother two metabolites also demonstrate asimilar trend between serum quantities andΔE from thecolor. Thefact that therewasadistinguishable differencevisuallyandquantitativelypoints to thestrongpredictive natureof usingΔEas ananalysistoolforstudying the presenceof metabolites in sputum. TheΔE value is nothing morethan thedifferencebetween the darkest shade and the lightest shadeof thesnaptaken, in the caseof poor lighting, there willbedifferencethat is erroneouslysmall whichcan bemisinterpreted. TheΔE value is beingusedas the variableinput into the JAVAapplet. This is preciselywhythe success of the JAVAappletis highlydependent on the lightingin theroom whereтheapp is used to be as close to sunlight(broad spectrum) as possible.

V. Useful Computational Results

When Adderallusersaswellas clean patients onthe samegraph, trends depictingapoor linear regression and averyslight slopebecame apparent on all plots made.This demonstrates the independent natureofthe data collected foreach of the3 metabolites. TheseΔE values are inputted into theJAVAapplet, theirindependent nature enables the algorithm to producea conclusive and definitivestatement about themetabolites present.

TheJAVAappletanalyzes the deltaE values, obtained via chromophore-metabolite reaction in thesputum, bycomparingthem to controls. ByusingDeltaE values to quantitatively measurepresenceof molecules, color detection technologycan move further from an opinioned personal belieftoamoretangiblemeasurement tool that can revolutionizethe waywesharedata. The assignment ofnumerical values tocolorenables programs like theJAVAapplet to take theseinputs and generatea conclusiveresultabout thedata. This will takethe responsibilityof decision making from thehands ofatired lab technician, into the objective algorithmic fingers of IT. Medical imaging, tissuecultures, heat measurement studies and manymore color-based assays used todaywillbeable to bebettercommunicated and therebyimproveinter- and intra-disciplinarycollaboration.

VI. Conlusions And Future Possibilities

Themethodologyof analyzingdeltaE values usingaJava-applet whichcompares experimental sampleto the control can not onlybeused to diagnoseAdderallin saliva, but also can beused to diagnoseheroin, cocaine orotherdrugs in saliva.If theright biomarkers arefound this methodologycan beused to detect anydrugin saliva.

Thenext step forthe salivatest would beto test outthe chromophore-molecule reactions in a lab, and to engineer thephysical saliva test strip.

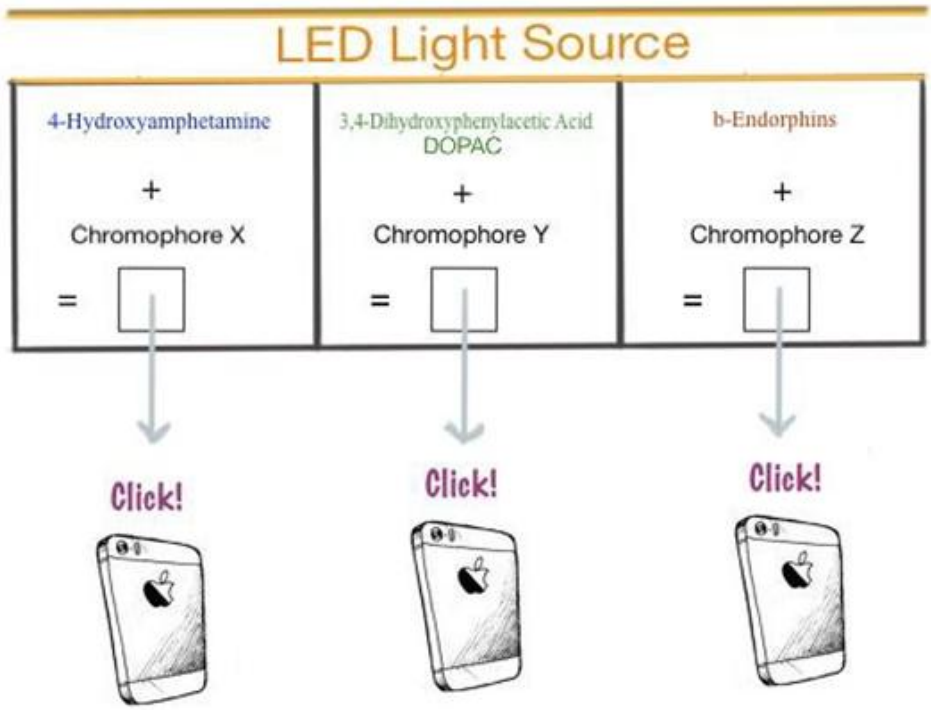

Figure 15: Modelofthe actualsaliva teststripthathas beenengineered usingthe methodologydeveloped inthis paper

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Appendices

```
importjava.awt.*;
importjava.awt.event.*;
importjava.applet.Applet;

importjavax.swing.JTextField;

publicclassGibbsextendsAppletimplementsActionListener
{
LabelALabel=newLabel("AlertMessage");                    TextFieldAlert=newTextField("Hello!");
Buttoncalculate=newButton("Calculate");
LabelHLabel=newLabel("Enthalpy,dH[Joules]");
TextFieldenthalpy=newTextField("Pleaseenterenthalpy",10);
LabelSLabel=newLabel("Entropy,dS[Joules]");
TextFieldentropy=newTextField("Plearenterentropy",10);
LabelTLabel=newLabel("Temperature°K");
```

```
TextFieldtemperature=newTextField("PleaseenterTemprature",10);
LabelGLabel=newLabel("GibbsFreeEnergy,dG[Joules]");
TextFieldenergy=newTextField("0",10); LabelSpLabel=newLabel("Spontaneity");
TextFieldspontaneity=newTextField("Equilibrium",25); Panelp=newPanel();
privatestaticbooleanvalid=true;

publicvoidinit()
{
setBackground(Color.white); p.setLayout(newGridLayout(4,3,3,3)); p.add(ALabel);
p.add(Alert);
p.add(TLabel);
p.add(temperature); p.add(SLabel); p.add(entropy); p.add(HLabel); p.add(enthalpy); p.add(GLabel);
p.add(energy); p.add(SpLabel); p.add(spontaneity); p.add(calculate);
calculate.addActionListener(this);
add(p); Alert.setEditable(false); energy.setEditable(false);
}


intgetValue(Stringstr)
{
intnumber;
try
{
number=Integer.parseInt(str);

valid=true;
}
catch(NumberFormatExceptione)
{
number=0;
valid=false;
}
returnnumber;
}


publicvoidactionPerformed(ActionEventevent)
{
inth=0,s=0,t=0,g=0;

StringHstr,Sstr,Tstr,Gstr,Spstr;

inti=0;
while(i<3)
{

Hstr=enthalpy.getText(); h=getValue(Hstr); if(!valid)break;
i++;

Sstr=entropy.getText(); s=getValue(Sstr); if(!valid)break;
i++;

Tstr=temperature.getText();
t=getValue(Tstr); if(!valid)break; i++;
}

switch(i)
{
case0:
```

```
{
Alert.setText("InvalidEnthalpyInput!"); Alert.setEditable(true);
spontaneity.setText("CannotBeDetermined!");
energy.setText("");
break;}

case1:
{
Alert.setText("InvalidEntropyInput."); Alert.setEditable(true);
spontaneity.setText("CannotBeDetermined!");
energy.setText("");
break;}

case2:
{
Alert.setText("Invalidtemperature."); Alert.setEditable(true);
spontaneity.setText("CannotBeDetermined!");

energy.setText("");
break;}

default:
{g=h-(t*s);
if(g==0)
{
spontaneity.setText("Equilibrium");
}

elseif(g>0)
{

happen)");

happen");

}
else
{
}
spontaneity.setText("ReactionisNonSpontaneous(Cannot
spontaneity.setText("ReactionisSpontaneous(Can

Gstr=Integer.toString(g); energy.setEditable(true); energy.setText(Gstr);
}

}//switch
}//ActionPerformed
}//classGibbs
```

Figure 16:Code forDelta EJava Applet

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